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FIFTY YEARS OF MEDICINE

SATURDAY JANUARY 7 1950

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BRITISH MEDICAL JOURNAL

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ADVANCES IN MEDICINAL THERAPEUTICS

BY

Sir HENRY H. DALE, O.M., G.B.E., F.R.C.P., F.R.S.

I think that our successors, viewing the times in which we live from the longer perspective of history, are likely to recognize the first half of the twentieth century as the period in which civilization first began to feel, for good or ill, the full impact of progress in the natural sciences. The application of scientific knowledge and methods to man's common activities and needs can be traced, of course, to much earlier beginnings; but the richness of the nineteenth century's closing decade in major discoveries, of the kind from which science advances with a fresh impetus and in new directions, seems to have caused a sudden acceleration of this process to begin about the turn of the century. In no department of knowledge and practice has this change, since 1900, been more conspicuous or more rapidly progressive than in the general field of medicine. The end of the nineteenth century found medicine still a body of largely empirical knowledge, growing mainly by slow accumulation from the direct study of disease at the bedside and of its results in the post-mortem room—a method which in that century had yielded rich harvests indeed; but these had been rare and had ripened but slowly. In 1900, when I entered upon my own undergraduate clinical studies, experimental research had begun to exercise an influence on clinical practice in certain directions, and especially on some aspects of diagnosis—several decades earlier, indeed, it had had Lister's revolution of surgical methods to its credit—but the relation, in general, between the laboratories and the wards remained one of critical aloofness on both sides. It was possible, and not unreasonable, for the student then entering the wards to receive, as I did, an authoritative warning that it was his duty to forget the teachings of the experimental science of physiology and to accept those of medicine, as still an empirical art. The upward inflexion of the curve of progress in the applications to practice of the results and the methods of experimental science seems, indeed, to have begun later in medicine than in some other directions; but when it came it was to be only the more abrupt in its onset, and the resulting revolution in the fifty years which followed was to be only the more complete. It seems to me, then, that a symposium on "Fifty Years of Medicine," from whatever different angles the separate contributors may approach the subject, must have as a central theme that revolution in its relations with the experimental sciences. This has led medicine not only to draw ever more freely from an ever-widening range of these for its own practical purposes but also, in the process, to be so permeated by their methods as to have become largely an experimental science itself well before the end of the period under review.

When I was invited to deal with "Advances in Medical Science" as my contribution to this symposium it seemed to me, accordingly, that acceptance of such a commission would oblige me to range far and wide over nearly all the changes which have occurred in medicine in the past fifty years, and to make deep inroads into almost all the allotments to other contributors. Even a superficial survey of a field so immense and so inclusive I judged to be beyond the proper scope of a single contribution, and far beyond the competence of a single reviewer. I could have written, indeed, with some knowledge, and with the best of reasons for gratitude, of advances in the general estimate of what medical research is worth and of what it can be expected to do. These have raised its status from that of a spare-time enterprise for the rare and unworldly devotee in 1900 to that of an activity to be encouraged and supported, as a career in itself for a minority having a special aptitude, but also as a desirable item in the experience and the credentials of every aspirant to distinction in clinical teaching and practice as we find it to-day. Any survey of the remarkable changes in that direction, and of their effects in enabling this country so greatly to expand its contribution to the general advance in medical science, would have to recognize the enlightened application of public funds through the Medical Research Council and, later, through the University Grants Committee also, as well as to the support given by great private endowments and organized public appeals to the charitable. All of these have been creations of the past half-century.

My proper task, however, was rather to give some impression of the nature and the extent of actual advances achieved in medical science, under whatever stimulus, since 1900; and the only practicable way of attempting this seemed to be to select for review, by way of illustration, the changes which have taken place in one of its major aspects. The developments in medicinal therapeutics seemed likely to serve this purpose particularly well; I doubt whether the change in the half-century in any department has been greater or more fundamental than in this. The interests of the laboratories and the wards seem here to have been even more widely divergent in 1900, and to have since become even more closely identified, than in most other aspects of medicine. I decided accordingly to limit my contribution to a consideration of "Advances in Medicinal Therapeutics"; but I am aware that, even so, there are likely still to be many points of common interest and inevitable overlap between this, my chosen field, and those with which several of my fellow contributors are to deal.

The remedies which were being administered in 1900 had almost all come into use as the result of empirical observation; their reputation in the majority of cases was based on practical experience and tradition, or even on vague general impression. The purpose of medicinal treatment was then generally held to be that of assuaging the symptoms of disease, leaving a radical cure, if any were possible, to the *vis medicatrix naturae*—how the pompous pedantry of the phrase recalls the atmosphere! "I don't pretend to explain it, but I have seen it do good," was a familiar reply to the student inquisitive concerning the reason for a prescription. The scientifically conscientious physician was frankly and cynically sceptical of the value of any but a few of these traditional remedies. Some of them—mercury, quinine, ipecacuanha—had, by chance, unrecognized actions of the type which we now call "chemotherapeutic" on the specific causes of different infections; others—digitalis, the purgatives, salicylates, morphine, atropine—had established values in the relief of urgent symptoms. Pharmacology concerned itself then chiefly with the finer analysis of the actions of remedies which tradition had thus brought into use; and even on those lines its potential contribution to practice was seldom readily obvious. There was at least some justification for the clinician's familiar gibe—"healthy frogs are not sick men"—as well as for the pharmacologist's lack of interest in a therapeutic practice which used so many drugs of no demonstrable actions for purposes so ill defined.

Already in 1900, however, there were signs from more than one direction of the great change that was on the way. Synthetic chemistry had already begun to intervene, with the production of new artificial remedies, though still on a relatively limited scale. I remember aspirin as a new product, designed to allow salicylic acid to pass through the stomach without risk of its irritating action; aspirin's mild analgesic, hypnotic, and diaphoretic actions were to be discovered later, and by patients, I believe, as much as by their doctors. On the other hand, there were signs already of a much more fundamental change, in the use of a few products of experimental research dealing directly with the causes of disease and not merely with its symptoms. Such were thyroid gland, which Murray had first used in 1891 on the basis of Horsley's experiments, to repair directly the deficiency of the gland in myxoedema and cretinism; and the diphtheria antitoxin, discovered by von Behring in 1891 and made practicable some years later by Ehrlich's more fundamental studies, a direct antagonist to the infective cause of that disease. Both these were established in routine use by 1900, though their direct activity and its scientific basis still gave them a special prominence and an interest of novelty against the generally obscure background of the traditional therapeutics. In 1900, also, Almroth Wright's typhoid vaccine, one of the pioneer preparations of this type, was on trial in the South African War. A discerning student of the literature might, thus early, have detected portents even of the coming of a specific chemotherapy of infections which was to have its effective beginning only a few years later, though the full range of its possibilities would not begin to appear till much more recent years.

I do not think that an adequate impression of the extent and the nature of this change in therapeutics which the fifty years have witnessed can be obtained without examining at somewhat closer range the course and the speed of the developments along each of these different lines. We have to consider the advances made in the immunological and the chemotherapeutic treatments of infections, and in the direct replacement of deficiencies, whether hormonal or dietary—all these belonging to a type of treatment, essentially the creation of this century, which aims at removing causes; and we must look also at the immense improvement in the range, the effectiveness, and the scientific credentials of remedies applied to relieve symptoms. In no case will it be possible to attempt more than a hasty outline, with details added here and there only by way of example, and not with any idea of presenting a complete picture.

Immunotherapy

The emergence, during the past half-century, of immunology as a practically new branch of medical, biological, and eventually of physico-chemical research and knowledge, with many secondary ramifications and growing-points, is altogether beyond my aim. I can attempt no more than a brief sketch, with many lacunae, of its practical effects on the treatment of infections.

Passive Immunization

As already suggested, it was the practical introduction, just before the turn of the century, of this specific method of treatment, and particularly the use of the diphtheria antitoxin, which started the effective development of immunotherapy. Less directly, it was to play a great part, indeed, in stimulating the search for remedies of other kinds which would also deal directly with the causes in diseases of infection. Diphtheria antitoxin stands to this day as the typical agent of passive immunization, and as still the most important example of its successful use. After its early success it became the principal subject also of experimental studies directed to improving the method of immunizing the animals, mainly horses, used for producing an antitoxin, so as to obtain sera of high natural antitoxic value, and then to concentrate the specific activity into the smallest weight of a globulin, or even of an antitoxic moiety thereof, and therewith into the smallest bulk of solution. The choice of this antitoxin for such researches was largely due to the fact that Paul Ehrlich, in an investigation which will always be one of the classics of immunology, had produced a quantitative method for determining the antitoxic value of any sample in units defined in relation to a stable standard of reference; and this method is still the most accurate of all such biological titrations. Incidentally Ehrlich had thereby effectively laid down the main principles governing all the standardizations by the use of biological tests, which have since provided a basis for the accurate dosage of many different types of the newer remedies. It is perhaps not yet quite certain whether Ehrlich's method of standardizing diphtheria antitoxin gives, by itself, a complete indication of the therapeutic action of the products of the most advanced methods for the concentration and refinement of this serum. There can be no doubt at all, however, that it created the possibility of so early a production of a good antitoxin, and so precise a measurement of its activity, that the first decade of the present century witnessed an impressive revolution in the treatment of diphtheria. From then onwards, in so far as public health administration could ensure the injection of the antitoxin in an adequate dose at the very beginning of the disease, it became possible to reduce the case mortality of diphtheria practically to zero. One of the worst of the spectres which had haunted the minds of parents and of the doctors attending their children up to the end of the nineteenth century had already been laid thus early in the twentieth.

Almost contemporaneous in discovery with diphtheria antitoxin, and second perhaps to it in importance among the agents of passive immunization, was tetanus antitoxin.

It proved to have little, if any, value for the relief of tetanus when once the symptoms had appeared; but its prophylactic value, if administered soon after the infliction of such wounds as were otherwise certain to have produced cases of tetanus, was early placed beyond question. The antitoxin was used in this way, and with very great effect, during the first world war. With it may be mentioned the sera specifically neutralizing the exotoxins produced by other sporing anaerobic bacteria, responsible for gas-gangrene. The immediate availability and use of these sera in the second world war was one factor in the great reduction of a threatening complication of soil-infected wounds; though in this, as in some other directions, immunotherapy was to be supplemented, and later largely to be superseded, by an effective chemotherapy. Curative sera containing antitoxins, or immune substances specifically combining with constituents of bacteria which do not form potent exotoxins, were prepared against the dysentery bacillus of Shiga, and later against a whole range of the antigenically distinct types of pneumococcus. The antidysentery serum had much use in the first world war. In the period between the wars, till after the middle of the 1930's, the use of the type-specific antipneumococcus sera had achieved a dominating role in the radical treatment of pneumococcal pneumonias, especially in the United States of America; though the successive isolation of further types of pneumococcus, each requiring its separate serum, had begun to raise doubts about the eventual limits of such a treatment.

The use of all these specific antibacterial sera, however, was to feel an increasing rivalry from chemotherapy when, in 1935, the extension of this type of treatment to bacterial infections began with the introduction of sulphanilamide and continued with that of its derivatives; and then, before these had yet been fully exploited, came penicillin and the other antibiotics, from 1940 onwards. How far the latter may eventually replace even diphtheria antitoxin is not yet clear. What has become increasingly obvious in recent years is that in dealing with such infections as those of diphtheria or tetanus the therapeutic ideal is not the use either of antitoxins or of antibiotics, to stop the infective process after the latter has begun, but an active prophylactic immunization of the whole population at risk with neutralized or modified forms of the respective toxins.

Active Immunization

The artificial production of an active immunity goes back to Jenner, and was applied in principle by Pasteur. The attempts by Koch, and by others less cautious than he, to produce it with his various types of tuberculin had been so little successful, and in some cases so harmful, that their main effect was probably to discourage for a time any further development along those lines. In any case, when the present century began the more general value of active immunization in human medicine still lacked a practical demonstration on a scale sufficiently large.

Bacterial Vaccines

Wright's typhoid vaccine, consisting of a suspension of the killed bacilli and providing an early example of that type, came just too late for its effectiveness to be fully displayed in the South African War. Before 1914 its value had been established, especially by trials on the Army in India; so that it was then ready to be applied and to produce a brilliant contrast between the almost negligible incidence of enteric fever in the armies of that, the first world war, and the tragic experience in South Africa, where the disease had been more fatal than the Boer bullets. Another vaccine of this type the prophylactic value of which seems now to have been well established, when the organisms from an antigenically specific culture are suitably prepared, is that of the cholera vibrio. A more general attempt to use, even curatively, vaccines of this kind, made from organisms responsible for a wide range of common and more chronic infections, including tuberculosis, had followed Wright and Douglas's demonstration of a specific "opsonizing" effect of serum from immunized subjects. The use of their "opsonic index" as a quantitative guide to such curative immunization did not find permanent adoption, but it imposed a much-needed restraint on excess in dosage at a time when its introduction had helped to create a wave of enthusiasm and of confidence in the potentialities of vaccines, which later subsided to calmer levels.

Another type of active antibacterial immunization involves the administration of a living culture of a strain of the tubercle bacillus rendered permanently avirulent by a special cultural treatment (B.C.G. of Calmette and Guérin). This has been widely used, first in France and more recently in Scandinavian countries, especially to immunize children of tuberculous parents and nurses and others specially exposed to risk of this infection. Much later than in these other communities, it had just become the subject of systematic trial in this country as the past half-century was drawing to its end; we must wait for the new one to show whether the results will be as favourable here as those reported elsewhere.

Toxins and Toxoids

Remarkable success in the prophylactic production of active immunity has been obtained by the use of the sterile soluble exotoxins of such organisms as those of diphtheria and tetanus, rendered innocuous by neutralizing them almost completely with their corresponding antitoxins or by a chemical treatment converting them into "toxoids," freed from the toxicity but retaining the specific antigenic properties of the toxins. The possibility of such immunization with a nearly neutral mixture of diphtheria toxin and antitoxin was shown by von Behring; but its first practical application on a large scale was due to the vision and advocacy of W. H. Park in New York City, and to Bela Schick's skin test with a small dose of diphtheria toxin, by which evidence could be obtained of the need of the individual for immunization and of its success when applied. Systematic trials by Sheldon Dudley on a controlled community of young naval personnel did much to establish the value of the method in this country. The toxin-antitoxin mixture has been followed by other forms of the immunizing reagent—toxoid (anatoxine of Ramon) produced by treating the toxin with formaldehyde, toxoid-antitoxin mixture, "floccules" specifically precipitated from such a neutral mixture, toxoid precipitated with alum—the list is unlikely yet to be complete. The matter of importance is the complete success of the immunization against diphtheria obtainable with suitably spaced injections of a good preparation of any of the forms of antigen. There are large communities already where the systematic immunization by such methods of all susceptible schoolchildren, with a growing acceptance of general immunization in infancy, has caused the complete disappearance of diphtheria. The experience of the city of Hamilton, Ontario, has often been cited. The incidence of and mortality from diphtheria there had shown for years but minor fluctuations up to 1925, when general immunization was instituted; and both fell then so steeply that in that large population there has been no death from diphtheria since 1930, and no case of the disease since 1933. Other

large cities on the North American continent can now show similar records. The organization and advocacy of such immunization by our own Ministry of Health in recent years have already been followed by a pronounced fall in the death rate from diphtheria, but we shall have no reason to be proud of anything less than the complete elimination from our country of this menace to the life of children.

An equally conspicuous success followed the systematic active immunization against tetanus of armies engaged in the recent world war. A suitable tetanus toxoid was available, and, when an adequate routine of spaced injections had been determined, the effectiveness of the immunization with it was complete. There were, indeed, a few cases of tetanus, and of death in its agony, among those men of the Forces who, yielding to a campaign of persuasion, had refused the protective inoculation. There is a similar campaign now to frighten mothers into refusing, for their children, the protective inoculation against diphtheria. Could any cruelty be worse than these, inflicted by people who believe themselves to be more than commonly humane?

Viruses

Immunization against ultramicroscopic viruses, using strains of modified virulence, had, in effect, been used already by Jenner and by Pasteur. The most successful application of the method in human medicine during the present century, since the existence of such viruses was recognized and their properties brought under full investigation, is probably the immunization against yellow fever, using a strain of the virus transmitted through mice. The solidity of the immunity which follows recovery from many natural virus infections encourages a hope of further successes with artificial immunization in this field. Statistically significant results, though as yet of doubtfully practical value, have been obtained in the large-scale attempts which have been made to immunize communities against the viruses of influenza. Veterinary research and practice appear to have had greater success, so far, with such methods, and it seems likely that more are yet due to be achieved by them in human medicine.

Chemotherapy

Even before the end of the nineteenth century Paul Ehrlich was laying plans to find artificial, synthetic remedies, dealing as directly and specifically with infections by protozoa as the new immunological remedies were dealing with infections by certain bacteria. Quinine, provided by nature, appeared to be such a "chemotherapeutic" remedy for the malarial infection; the project was to discover by artificial synthesis other more potent and less toxic remedies, with an even stronger specific affinity for the infecting parasites and an even weaker one for the organs of the infected host—substances more "parasitotropic" and less "organotropic." Ehrlich had indeed begun this quest with Guttmann as early as 1891, when they tried methylene blue as a remedy for malaria; but it was abandoned for the time on account of the impossibility of systematic research, when only occasional cases of malaria, and those in man, were available as subjects for the trial of potential remedies. The real opening of the campaign began with Laveran and Mesnil's discovery that trypanosomes responsible for various animal and human infections in the Tropics could be maintained indefinitely, by serial passage, in rats and mice. Ehrlich seized the opportunity and, with the Japanese bacteriologist Shiga, he had discovered by 1903 a benzidine dye which they named "trypan-red," because of its definite curative action on these laboratory infections of rodents with trypanosomes. I was myself in Ehrlich's laboratory about the time when this discovery was ready to be made public. It provided the real point of departure for the new scientific adventure of chemotherapy, the development of which, still in vigorous progress, has provided one of the most romantic of all the chapters in the story of this century's achievements in therapeutics.

Dyes and Similar Synthetic Substances

Trypan-red itself did not justify its first experimental promise when it was tried for the treatment of naturally acquired trypanosomiasis in man and the larger animals. Apart from its general and symbolic significance, however, it had a more direct one. It served as the particular starting-point for a series of researches on dyes and substances with comparable structures which culminated, after Ehrlich's death during the first world war, in the discovery, by a team in which his former pupil Roehl was a leading member, of a complex colourless substance named "germanin" by the industrial laboratory in Elberfeld in which it was made, and where its properties were revealed. In this country it has since been made under the name "suramin," and it is probably the best practical remedy yet discovered for the trypanosomal sleeping-sickness of man.

Arsenical Remedies

It will be impossible here to follow in detail the various lines along which chemotherapy has had its effective developments. It must suffice briefly to mention some of the more successful and important. One clue to a new line of advance was provided by the discovery made by Thomas and Breinl, in Liverpool, that the organic derivative of arsenic acid, long known by the trade name "atoxyl," was a more potent remedy for laboratory trypanosomiasis than arsenic in inorganic form. Discovering the true formula of atoxyl, making a more intimate study of the nature of its action, and using further the knowledge acquired in 1905 of syphilis, as due to infection with a spirochaete, Ehrlich and his co-workers arrived by 1909, through many stages, at the arseno-compound which they called "salvarsan." They demonstrated its outstanding activity against spirochaetal infections, and thus for the treatment of syphilis, and chemotherapy therewith attained its first great practical triumph. It would be difficult to exaggerate the effect on medical opinion throughout the world of this first success in producing, by an experimental research organized to that end, a specific remedy, acting directly on a disease of such importance as syphilis, and so rapidly effective that, when it was used at an early stage, an infection hitherto so resistant could be eradicated by a short course of treatment. It would be impossible here to attempt even a sketch of the modifications and improvements which this treatment has undergone; the most recent is the use, in repeated fractional dosage, of the arsenoxide which had formed the last step but one in Ehrlich and Bertheim's synthesis of salvarsan.

An immense stimulus was given by this success to the extension of chemotherapeutic researches in other directions; but for the next quarter of a century the further major successes were relatively few, were practically restricted to the treatment of infections due to protozoa and to spirochaetes, and were thus predominantly concerned with diseases of the Tropics.

As another and later practical outcome of the line of research which, starting from atoxyl, had progressed through arsenophenylglycine to salvarsan (arsphenamine),

mention should be made of tryparsamide, the result of researches in the Rockefeller Institute, New York, which seems to have shared, so far, with germanin (suramin) the leading role in the practical chemotherapy of human trypanosomiasis.

Antimalarial Remedies

The Elberfeld laboratories, where methods had first been elaborated for using the malaria-like infections of small birds for preliminary trials, produced two valuable synthetic remedies for human malaria, "plasmochin" ("plasmoquine," pamaquine) in 1926, and "atebrin" (mepacrine) in 1930. The latter was to be successfully exploited by an Anglo-American war effort and to be given its first large-scale trial and systematic investigation when Japan, early in 1942, had seized the world's main sources of quinine; and it was thus to become a factor of very great importance in the fighting strength of the forces by which Japan was ultimately defeated. And meanwhile a co-operative and systematic effort, made also by British and American workers during the war, to find further and better antimalarial remedies had produced several; that contributed by a British team, "paludrine" (proguanil), showing outstanding qualities of low toxicity and efficacy against certain strains, at least, of malarial infection. This availability of effective antimalarial drugs became an important aid, moreover, to new and still actively progressing investigations on the natural history of the malarial infections in man; with the result that the attack on the malaria problem, which even up to the outbreak of the recent war had progressed but little beyond the stage of attempts at mosquito control and quinine distribution, has now at disposal a wealth of new knowledge waiting to be fully exploited, and to produce, it may be hoped, a new and more rapidly progressive phase of this campaign in the new half-century.

Other Protozoal Infections

There are many other examples of the chemotherapy of protozoal infections which would deserve mention for their interest and importance, but I must be content merely to note the successful treatment of *Leishmania* infections, the heavily fatal kala-azar in particular, by organic compounds of antimony and by the purely organic long-chain diamidines.

Chemotherapy of Bacterial Infections

The most remarkable feature, however, of this intermediate period of some twenty-five years was that hardly any success, and none of a practically convincing character, had resulted from many attempts to extend chemotherapy to the ordinary bacterial infections. Ehrlich had encountered an early check in this direction, and the renewed efforts of those who followed him had fared but little better; so that an opinion had come to be held, and seemed to be hardening into a conviction, that, except for certain widely spread spirochaetal infections like syphilis, the prospect for chemotherapy would still be limited to the treatment of protozoal infections and therefore chiefly to that of tropical diseases; while immunology, it seemed, must continue to provide the specific remedies for the bacterial infections predominant in our temperate climate. Then, in 1935 and the years immediately following it, this picture changed completely; the scope of chemotherapy underwent a greater and more rapid expansion than any which had gone before, and with strong reinforcement by a new advance from another direction it continues to this day.

Sulphanilamide and its Derivatives

It was in 1935 that Domagk, of Elberfeld, published his evidence of the effective action of the red dye "prontosil" against streptococcal infections in a number of human cases as well as in experimental mice. Soon there followed the demonstration by Trefouël and his colleagues in the Pasteur Institute, that the much simpler colourless moiety of prontosil, sulphanilamide, was the directly antibacterial agent; and then, in 1936, the first controlled and systematic trial of both prontosil and sulphanilamide, by Colebrook and his team in London, on a series of comparable cases of streptococcal septicaemia. The result put the importance of the discovery beyond question. In 1938 the development of the series of sulphanilamide derivatives began, with Whitby's description of the superior activity of sulphapyridine (Ewins and Phillips) on pneumococcal infections. Clinical trials of this derivative followed, and spread soon to meningococcal and gonococcal infections: and the new order of the success of this treatment was so clear, in all these conditions, that the fame of it began to reach a wider public. Then in rapid succession followed sulphathiazole, sulphaguanidine, sulphadiazine, sulphasuxidine, and the rest—each with its special advantages or its more specific value for certain types of infection. Thus the prospect of sufferers from a whole range of the commoner bacterial infections was transformed in a few years. There were many conditions with which, in default of an effective antiserum, the physician had been restricted to a merely "expectant" treatment or an opportunist attempt to ameliorate symptoms; he now had medicinal weapons to attack the causes of such illness

Antibiotic Remedies

Long before the possibilities of the sulphanilamide series had been fully developed another chemotherapy of bacterial infections became available, from a quarter widely separated from the synthetic approach envisaged by Ehrlich and so far adopted by his successors. The story has so often been told that it need not be repeated here in detail, of Alexander Fleming's discovery of penicillin through the action of a mould-colony which by accident contaminated a plate culture, and of his partial exploration of its properties in 1929; and then of the new initiative of Florey, Chain, and their co-workers in 1939, which led to its purification and the demonstration of its outstanding practical value as a therapeutic agent, in the first instance for the treatment of infections by staphylococci. The joint achievement, with all that flowed from it, seems certain to rank as one of the main events, with an influence as powerful and far-reaching as any, in the whole history of therapeutic research and its applications. War's urgency had much to do with the rapidity of the development from laboratory experiment to large-scale production; and with the resources thus made available, and an intimate co-operation of leading scientists of the U.S.A. with those of our own country, came the separation of penicillin into several closely related compounds, the determination of the structure of these, and even, in the case of one, the confirmation of that structure by artificial synthesis on a small scale. All these scientific developments, too, were attained with a rapidity which a prognosis based on the standards of peacetime might well have dismissed as incredible.

Penicillin soon proved to have therapeutic applications, first to problems of infection to which war gave special prominence, and then to those of a commoner urgency in peace, far beyond the range of any which would have been predicted. It was soon found to be an effective

remedy for syphilis, as well as for a wide range of bacterial infections. Its actions thus extensively supplemented as well as overlapped those of the sulphanilamide series and even of salvarsan. There were still bacterial infections, however, particularly among those due to Gram-negative and acid-fast bacteria, with which none of these could deal adequately. The filling of these gaps was soon to begin, however, through the rapid exploration of the therapeutic possibilities of a large series of other antibiotic products, to which the brilliant results obtained with penicillin had given so effective a stimulus. What has already been achieved in this direction with streptomycin, "chloromycetin" (chloramphenicol), and aureomycin is matter of a history still in the making. Each of these can claim effective activity against some of the types of infection which had shown resistance to penicillin, as well as to the sulphanilamide derivatives and other chemotherapeutic agents. The evidence that streptomycin will cure tuberculous infection in its acuter and more generalized forms, important in itself and as providing the first clear evidence of the possibility of directly and rapidly eliminating an infection of that kind, opens also a new vista of hope, at least, for the eventual discovery of a similarly effective chemotherapy for the much commoner localized and chronic manifestations of tuberculosis. Chloramphenicol, with its chlorine content and simple structure, which has enabled it already to be produced on a practical scale by synthesis, has among other actions a direct and rapidly curative one on infections due to organisms of the *Rickettsia* group—typhus and related diseases—raising possibilities which till recently had seemed to be almost outside the range of any reasonable ambition. For the rickettsias, obligate parasites with no power apparently of extracellular growth, seem in their dimensions also to be intermediate between the smallest bacteria and the true viruses. With aureomycin the successful treatment of some true viral infections has already been claimed. So that an effective chemotherapy of this range of infectious diseases has come now to be regarded as a likely development, even in the early years, perhaps, of the half-century now beginning.

Replacement of Deficiencies—Hormones and Vitamins

Hormones

The high hopes raised by the treatment of myxoedema with thyroid gland in 1891 that similar successes would be obtained with other ductless glands were to encounter a long disappointment. The isolation of adrenaline (epinephrine) near the beginning of the century had no important bearing on Addison's disease; and the next hormone to be isolated, thyroxine (1915), was concerned with the one endocrine treatment which had already succeeded. The other endocrine extract to be used with success in therapeutics, that of the pituitary posterior lobe, had first been used, like adrenaline, for its symptomatic effects, and not for the repair of any known hormonal deficiency; though its antidiuretic hormone was eventually to be applied in a true replacement therapy of such a defect in diabetes insipidus. A suspicion had begun to grow, and to strengthen with the passage of some thirty years, that if the other supposedly endocrine glands really produced internal secretions the active constituents of these might be so little stored in the glands, or so unstable, as never to be accessible for direct investigation, or for effective application in treatment. The whole outlook changed in 1921, when the courage, skill, and determination of Banting and Best demonstrated the possibility of separating insulin from the pancreas. This provided another of those landmarks, or points of new departure, in the field of experimental therapeutics of which we have noted several already; for from that point onwards the atmosphere of therapeutic research on endocrine organs and functions became one of renewed optimism and enterprise. One by one, active preparations from different endocrine glands—parathyroid, suprarenal cortex, gonads, pituitary anterior lobe—were obtained and applied in therapeutics and in further researches. The process of separating the hormones of the anterior pituitary lobe, each acting separately to excite the production or the output of the hormones of another of the endocrine organs, is a matter of special therapeutic interest at present. For one of these anterior pituitary hormones governs the hormonal functions of the suprarenal cortex, including the production and output of the hormone "cortisone"; so that the adreno-corticotrophic pituitary hormone (ACTH) has been used successfully as an alternative to cortisone in that treatment of rheumatoid arthritis which has recently provided a natural focus for so much eager attention. Here again, as the new half-century opens, we seem to be at the beginning of another new chapter in therapeutics, and are wondering what its later paragraphs may contain for us.

Vitamins

The treatment of scurvy with fresh fruit and vegetables seems to have been discovered and rediscovered in each of several earlier centuries, and even the use of cod-liver oil for rickets had long been recommended empirically. The recognition, however, that a natural diet contains small quantities of a number of accessory factors, to which, so inappropriately in the case of many of them, the general name "vitamins" has come to be applied; and the exact knowledge of the diseases of deficiency resulting from the lack of one or other of these in the diet; all these are achievements entirely of the present century. The paper by the late F. G. Hopkins, from which many would date the beginning of systematic investigations in this field, was not published till 1912. E. Mellanby's investigation producing the first clear evidence that rickets was due to the lack of such a factor in the diet, and that this was a fat-soluble vitamin such as cod-liver oil contains, was published just after the first world war, in 1919. All except the most recent items of the great complex of investigations, by which the vitamins responsible for different aspects of normal growth and metabolism have been chemically isolated and identified, were carried out in the two decades between the two world wars. Till that period, indeed, there had been a tendency to think of the vitamins, like the hormones, as probably present in traces so minute, or as so unstable, that there might never be a reasonable prospect that any would be isolated and chemically characterized. The most recent isolation of a substance belonging to these groups came in 1948, with the practically simultaneous isolation in the U.S.A. and in England of the so-called vitamin B_{12}—the haematopoietic principle of the liver, acting in doses of only a few micrograms to replace the factor missing in pernicious anaemia. It is characterized by the presence of cobalt in its molecule, and might be regarded as either a hormone or a vitamin; and its discovery makes interesting contact with a large body of work on trace elements in the soil and their significance for the growth of vegetation and the health of the stock nourished by it.

Artificial Synthesis

Just as the 1920's may be regarded as the golden decade for the separation of different hormones and vitamins, the 1930's were, in both ranges, that for structural identification

and artificial synthesis. In astonishingly rapid sequence a whole series of hormones, chiefly sterinoid hormones of the gonads and the suprarenal cortex, were thus made artificially from 1930 onwards; Harington's work had led him to the synthesis of the iodine-containing thyroxine already in 1927. From 1930 again, the synthetic production of a series of vitamins with a wide variety of chemical characters came with a like rapidity. In a number of instances the syntheses were applicable on a large scale; so that substances which but ten or fifteen years earlier had still been regarded as doubtfully accessible to any accurate chemical study became now available in quantity for practical use in the prevention or cure of diseases of deficiency, whether hormonal or dietary. The close of the half-century has found expectation keenly alive to the potential significance for therapeutics of an economically practicable synthesis for cortisone, or, perhaps, for the anterior pituitary hormone governing its natural output.

Remedies affecting Symptoms

The past half-century has also witnessed a very great extension of the range and the variety of the remedies available to control or modify symptoms, to ease pain, to induce sleep, and to curb or to stimulate natural activities. These developments have, indeed, a less revolutionary aspect than those discussed in the foregoing sections, in that they have involved no radical change of therapeutic aim from that which predominated in 1900, but mainly an immense increase of efficiency and of recourse to experimental guidance in its practical realization. Apart from opium, morphine, and cocaine, the resources available for analgesia or local anaesthesia were very meagre when the century began: sulphonal was then a standard hypnotic, and the materials available for surgical anaesthesia had changed remarkably little since Simpson introduced chloroform. The barbiturates, basal anaesthetics in general, the range of anaesthetic gases and vapours now available for inhalation, the variety of synthetic substitutes for cocaine and of the methods of applying them—all these are creations of these fifty years. The patient who at first hand can compare the methods of induction and the after-effects of the surgical anaesthesia of thirty, or even of twenty, years ago with those experienced under the best conditions now available will be at least as conscious of the contrast as is the anaesthetist or the surgeon.

It would, of course, be quite impossible to attempt even the most superficial review of changes and innovations in the whole of this vast field. The full enlistment of the powers of synthetic chemistry, and the combination of these with commercial enterprise, have doubtless had the result, in many directions, of producing a redundance and of presenting therapeutics with a bewildering choice of alternatives. Altogether, however, and in comparison with what was available when the century opened, the result is beyond doubt an enormous enrichment in materials for use in effective treatment, whether these are externally applied, swallowed, inhaled, or given by injection. Overlapping into diagnosis, similar methods have produced a range of substances giving contrast shadows of organs and systems by *x*-ray photography—a method of which the very basis was a novelty in 1900. Altogether, the main change to be observed in fifty years in the therapeutics dealing with symptoms is the rapid replacement, here also, of empiricism and tradition by methods and remedies based increasingly on the knowledge offered by experimental research. Let me mention but two recent examples of development in that direction, chosen out of a truly immense number available for citation.

Curare and its action have been known since Claude Bernard investigated them a century ago. It is only recently, however, that it has become possible and safe, through a detailed understanding of the method of its action and the means of correcting an excess of this, and through the availability of a pure *d*-tubocurarine, to use it as an adjuvant to surgical anaesthesia giving muscular relaxation; and it has thus become possible to reduce the quantity of the essential anaesthetic to the amount required to secure unconsciousness alone. And now there is news already of at least one synthetic substitute even safer and more effective than any natural curarine; and, since the search began but a few years ago, there are possibilities yet of much further advance.

Experimental evidence, accumulating since 1910, had shown that the symptoms of an allergic reaction are largely due to the action of histamine, released from sensitive cells when the allergen combines with an antibody attached to these. And now there is offered a large and growing series of synthetic substances which can be used to suppress or ameliorate an allergic reaction, by their direct antagonism to the action of histamine.

And these are but examples of a general tendency which in the past half-century has lifted this treatment of symptoms also to a higher plane of scientific sanction and experimental discovery.

Conclusion

Look back, those who can do so, to the beginning of this century, and recall again the state of medicinal treatment fifty years ago. Heart tonics, purgatives, diaphoretics, analgesics—such, indeed, were in use, and could be reasonably credited with the promotion of a natural function, or the relief of a distressing symptom; but there was a wide range of remedies then still current for which nothing more definite than a generally "tonic" or even "alterative" action could even be suggested. The idea that a remedy could directly remove or neutralize the cause of an illness was still a startling innovation, and neither physician nor patient had yet learned to expect a medication which would go thus to the root of the trouble. Compare such a position with that to-day, when we have become so accustomed to the effective and radical treatment, or prevention, of diseases which till recently were beyond the reach of remedy that there is a tendency to regard the existence of others as a reproach, as well as an incentive, to medical science. Rickets, scurvy, myxoedema, diabetes, pernicious anaemia, syphilis, pneumonia, coccal meningitis, dysentery, typhus—these are no more than a sample from a list which could be made of diseases now brought under such rational and effective treatment that the whole attitude to them, of the public as well as the profession, has been radically changed. It can hardly be doubted that this aspect of medicine, at least, has been the subject of a greater advance since this century began than in all the centuries which went before it. Members of the public who remember the position even thirty years ago, and recognize the contrast between the prospects of sufferers from diabetes, say, or pneumonia, then and now, not unnaturally inquire when anything similarly effective is to be expected for cancer or poliomyelitis or the common cold. The proper reply is surely that, though therapeutics as an experimental science is now on the march, it has only begun to get into its stride. We who have been able to watch the beginning of this great movement may be glad and proud to have lived through such a time, and confident that an even wider and more majestic advance will be seen by those who live on through the fifty years now opening.

SURGERY 1900-1950

BY

GEOFFREY JEFFERSON, C.B.E., M.S., F.R.C.S. F.R.S.

Professor of Neurosurgery, University of Manchester

It must be understood that I have no hopes that these lines give more than a bare outline of the advance of surgery during the past fifty years. Life is too colourful, too many-sided, and too rich to allow itself to be pictured in a few words or for anyone to catch the likeness of an age in a few happy sentences. Samuel Maitland once said of the writing of history that its essential matter was not what happened but what people said and thought about it, and in our time Toynbee holds that facts never speak for themselves, ideas being the machine-tools of the mind, the clues of motive and of action. So, in attempting to attach values to the progress of surgery during the first half of the present century it should be the scientific theories, the applications of discoveries, and the humanistic concepts proper to them to which we should most attend. And since they all emanated from people it is impossible to avoid making this story largely that of individuals.

Everyone is so well aware of what are the surgical activities of to-day that these need no detailed advertisement, and indeed so great are they that the history of each separate branch of surgery in this period of survey would make a sizeable book. And in writing these words, "in each branch" of surgery, the idea comes to mind that it might be more worth while to look back at what was happening fifty years ago than to attempt a comprehensive description of what is happening now, a review that would fail to do either justice or honour unless it were undertaken by a whole brotherhood of particular specialists. We should together be able to say that the years 1900–1950 were characterized by a great advance in certainty, in assurance, and in understanding of the natural history of pathological entities.

Once the prejudices against operation had been overcome (and important objections came from estimable people within the ranks of the profession—notably in thyroid diseases) it became possible to observe disease processes in their early stages before the development of those complications that formerly brought them to the post-mortem room. Moynihan, of course, summed this up in one of his popular phrases, "the pathology of the living." Again, one of this master's dicta, "We have made surgery safe for the patient, we must make the patient safe for surgery," would almost suffice as a motto for the age. But the times when persons believed that verbal felicities could either solve serious issues or unravel a scientific uncertainty are past; the spell-binders are gone.

These great men of the past—Moynihan, Murphy, the Mayo brothers, and George Crile, and some of the Continental leaders, about whom it is impossible to write without almost Dickensian hints of caricature in spite of the intense seriousness of their purpose—have few if any counterparts among the more serious and less flamboyant figures of to-day. Notwithstanding, the conception that surgical therapy consisted in a great deal more than the actual operation itself has been one that this century invented, with emphasis on post-operative care (and here I must recall the beautiful work of W. Pasteur (1913) on acute lung collapse after abdominal operations) and then, later, on preoperative. Moynihan, who was despite his conceits a very great man, had much to do with both of these advances, as has just been said.

Surgery Fifty Years Ago

Let us, however, return to our purpose and look at surgery as it was fifty years ago. A man surveying the previous fifty years at the end of 1899 must necessarily have found it an intensely exciting period to look back upon, more so in most respects than our own. There is not much that we do to-day that surgeons were not doing then; we do things better and more often, technical inventions allow us to be more venturesome, more exact, and more successful, we have new aids that they were denied. But since the 1880's something almost magical had happened, the release by Lister's work of surgery from the bondage of wound infection. The speed with which the new principles were applied derived from the fact that the surgical world already knew what it ought to do, and had been impatient to take advantage of safety when it came. I imagine that if anyone were given the choice of the most fertile fifty-year period the best would be 1880–1930.

The first successful gastrostomy had already been done in 1875, the first successful gastrectomy by Billroth in 1881, Mikulicz first sutured a perforated gastric ulcer, whilst posterior gastro-enterostomy had been introduced by von Hacker in 1885. The Murphy button had been invented in 1892, the Robson bobbin the same year. In 1903 total gastrectomy had already been done 16 times and with 10 recoveries, as Moynihan recorded in his description of his own first and unsuccessful case. Surgery was therefore well under way. Lawson Tait had done the first successful cholecystotomy in 1879, a fact remarked on by D'Arcy Power (1913) in his review of his own series of 73 cases between 1900 and 1912, but in 1908 Kehr had already collected 2,494 gall-bladder operations, many of them having been operated upon before 1900.

The only real difference in the statistics now is the great increase in numbers and the low mortality brought about by better diagnosis and earlier operation. Bland-Sutton recalled a successful splenectomy of his own done in 1895 and remarked on the improvements in the choice of cases for splenectomy, which he dated from 1890. Mayo Robson in 1903 could already review a personal series of 2,000 abdominal operations over a thirty-year period. He had 600 operations on the gall-bladder to his credit and had taken stones out of the common duct in 150, in the last 50 with a mortality of only 1.5%. He had performed 103 posterior gastro-enterostomies, with 3.8% of deaths. Mayo Robson mentions W. W. Keen's collected series of 20 cases of partial hepatectomy with two deaths, and Sir Henry Morris's 34 nephro-lithotomies with 33 recoveries. Robson himself had removed the kidney 112 times since 1892 with three deaths. In the pelvis, following on the lead given by Clay, of Manchester, in the 1840's, ovariotomy became so safe that Lawson Tait in 1885 had 139 cases without a death. The ruptured bladder had been sewn up, with recovery of the patient, by Sir William MacCormack, whilst Sir William Macewen and Sir Victor Horsley had already shown that notable successes were to be won even in the difficult terrain of the central nervous system. We have in fact to this day hard work to equal Macewen's results in brain abscesses.

The Great Wars

It would be fair comment to say that surgery had already advanced on a wide front and at great speed when the nineteenth century closed with the death of Sir James Paget. The practice of asepsis championed by von Bergmann was beginning more generally to supersede the strict Listerian ritual, and the prevention of wound infection had

reached a high enough level of efficiency at the outbreak of the first world war for surgeons to be able to look forward to the surgery of battle casualties with great confidence. How utterly their expectations were upset is now an old story. An aseptic technique went no further than the avoidance of implantation of new contaminants into wounds already deeply mired. The surgeon's pride was quickly humbled and he was soon listening with eagerness to anything that bacteriologists such as Sir Almroth Wright, Sir Alexander Fleming, and Leonard Colebrook could tell him not only about germs but about antiseptics. It was clear that experience in civilian practice had unfitted surgery for the case of grossly infected wounds, and we had to turn back in our tracks to Listerian principles.

The second world war at last found us with improved bacteriostatics and especially with the antibiotics that mankind so far had lacked, the latter because of the inspired observations of Fleming and the ingenuity and determination of Florey. This time there was in the end a different tale to tell, one in which only the first few chapters have been written, for the quest is not yet over. But that we have progressed so far as we undoubtedly have in the arrest of pyogenic processes is something of which all branches of medicine can be proud; the surgeon because, although he owes the new substances to others, their correct application remains his own proper work.

The occurrence within the last fifty years of the two most far-reaching wars that mankind has had to fight is of course this century's most important feature. In the South African War, still unfinished at the beginning of the century, the debonair figure of Sir Frederick Treves (so well depicted in the famous "Spy" cartoon) typifying the age—confident, trim, competent, adventurous, relatively wealthy, and extremely independent, doing what he could for the wounded in an Army that found the difficulties of Spion Kop and the Tugela River beyond both its experience and its expectation. But, like the Franco-German War thirty years before it, its surgical lessons, unlike its epidemiological, did not deeply impress practice.

Out of the two cataclysms that followed came very definite and permanent profits to offset a fraction of the misery and losses that they inflicted on mankind. The problems of infection have been mentioned, but there were many other gains: the institution of blood transfusion as a matter of vital and everyday consequence, a new insight into the intricacies of surgical shock, the care of fractures as a matter for trained specialists, and, perhaps above all, the value of team-work and the formation of teams embracing not only the actual operations but the treatment and management of disease generally. So firmly had team-work been established in the twenty years between the two great wars that the second found us not only materially but intellectually vastly better equipped to meet the even greater challenge. How well it was in fact faced and dealt with not only by the Services but by the E.M.S. of the Ministry of Health is a subject of such recent memory as to require no comment; the "Medical Histories of the War" when they appear will set it all on orderly record.

The Age of Specialism

The mention of team-work brings to the forefront something else, something that has been, as a generalization, a most characteristic feature of the past fifty years—the rise of the surgical specialisms. It has been those that have most sharply pointed the team spirit. If the period has to have proper names one would be the "Age of Specialism," but since specialization has been the natural outcome of increased knowledge and of surgical skills it will be remembered as no more than the first half-century of something permanent. Most of those who deplore this alteration, this production of branches by a growing trunk, have nevertheless realized its inevitability. But it will do no harm to recall that the necessity for specialization was already clear to some as far back as the 1890's.

In his 1895 Address in Surgery at the Annual Meeting of the British Medical Association, Jonathan Hutchinson strongly urged it. He made a review of the expansion of surgical activities since the 1850's, when, he said, one operating day a week sufficed for most of the great hospitals of London. Even in the 1900's the same room frequently did duty as both lecture hall and operating theatre. In company with Spencer Wells he had published in statistical reports in the *Medical Times and Gazette* each three months during 1856–1858 the operations and their results in London's important hospitals. The commonest operations had been for amputation, for breast tumours, and for strangulated hernia, of which last over 50% died. In addition, in a three-months period, of 13 lithotomies 3 died, and of 6 lithrotrities 2 died. Arterial ligatures were relatively rare (in contrast with the popular idea of those times now). But in 1857 Erichsen had successfully removed a ruptured internal semilunar cartilage, and Fergusson was not only excising upper jaws but fashioning new noses.

During forty years not only had the mortality of all operations fallen in a most encouraging way but the rarities had become commonplaces of everyday performance. Success rather than failure had become statistically probable. But how was a man to keep pace with the new development, to be equally skilled in everything? It was clear to Hutchinson that he could not pretend to be—what was more, that it would be wrong to make that pretence. As an illustration he took the treatment of stone in the bladder. He had, he said, been very successful with cystotomy for this condition, but of late years some surgeons had acquired great dexterity at crushing stones and washing out the fragments (Bigelow's litholapaxy). His own attempts at the new operation did not satisfy him, so he handed future cases over to a colleague adept at the new practice. He then made a remark which is as ingenuous and as sincere and as wise as any saint's—"I assure you that I regard the results of my practice in this department ever since I ceased to operate with my own hands with the utmost satisfaction and pride." The Victorians were not wrongly called great! For that is the statement of a great man, and it epitomizes the basic necessity for specialization.

The plea in reverse was also given by Hutchinson by his recalling a certain Mr. Gutteridge, of Birmingham, who claimed that he ought to be made "Lithotrotist to Great Britain" for the sublime reason that he performed the operation better than anybody else. How many of us have sheltered Mr. Gutteridge's ghost in our hearts for brief periods until some disaster shattered our pride? But it is not only because so many operations are done much better by the few but because they are done so much worse by the many that specialism has taken root.

Some special hospitals had already come into being in Hutchinson's day, chiefly in London, but many were in the Provinces. They were for diseases of the eye and ear, for obstetrics and gynaecology (with a now old-fashioned distinction between the obstetric physician and the gynaecological surgeon), for nervous diseases, for chest and heart affections, and for skin and venereal disease. Great though their contributions have been and still are, we would to-day rather see them not only as part and parcel

of general hospitals but on the same site, a commonwealth sharing staff and exchanging opinions in daily communion.

Abdominal Surgery

The specialisms within the corpus of what had hitherto been general surgery were more crisply defined in the second half of our fifty-year period than they were in the earlier years. Before the first world war and just after it British surgery was much influenced by trends which might or might not survive, inspired by individuals. Notable among these were the work and personality of Arbuthnot Lane. He had brought asepsis, especially in the plating of fractures, to a singularly high pitch, having developed a "no touch" technique in which nothing but the instruments were put in the wound. Lane was an ingenious, inventive man, as his work generally showed, not least in his explanation of the effect of skeletal stresses on bone shape and formation. When he carried this into the abdomen and pointed to the peritoneal bands and folds as protections against gravity which often overdid their purpose and caused chronic obstruction, reason outran common sense.

"Intestinal stasis" was held to be the clue to the cause of many diseases and the explanation of a horde of abdominal discomforts. This led to a riot of operating by and on neurotics either to divide bands, to remove colons, or to fix organs. It was the era of theoretical anatomy run mad whilst her sister physiology, who knew the answers, slept; they lay in neuromuscular mechanisms, as Cannon and Alvarez reminded a surgical world temporarily deaf. The Lane period in surgery would have delighted a Voltaire. Everyone was infected by it, but some had the disease much more lightly than others and were thereafter immune, and of it all Wilkie's duodenal ileus seems to be the sole but very uncommon survivor.

A notable sceptic to Lane's doctrines was Berkeley Moynihan, at his best in those years before an unparalleled wordly success had had time to spoil him. It was Moynihan with his gifts as a surgeon who first really created the specialism of abdominal, and especially of upper abdominal, surgery. Here was a man with all the qualities, intelligence, ambitions, devoted, indeed dedicated, to his art, extraordinarily dexterous as an operator, and persuasive to a degree. Under his leadership abdominal surgery fairly jumped ahead, and very considerable additions were made to knowledge of the earlier stages of visceral disease, "the pathology of the living." It was his boast that he had shown the way to make abdominal operating as safe as it could well be. There were critics who said that this had been an ill-service to mankind, encouraging useless and unnecessary operations. It cannot be doubted that to this day there are too many abdominal explorations, although the teaching centres have rid themselves of this pest. Diagnosis has become more certain thanks to the aids of biochemistry, radiographs, Graham's test, intravenous pyelography, and so forth, but not least a close study of the patient himself and of his body fluids.

Greater knowledge of the natural history of the ulcerative and infective processes of the gastro-intestinal tract has played a large part in redressing the balance. In fact, the part that applied physiology has played during the past few decades has been a powerful one. For instance, when the 1900's commenced, the recognition and operative treatment of appendicitis was a burning question, but the battle was soon won thanks to the brilliant teaching of Murphy, Treves, and others. Soon every young surgeon throughout the world was doing great service, but it remained for more recent years to invent the answers to the complications of appendicitis, general peritonitis, and ileus in particular. Even more revolutionary has been the preliminary management of intestinal obstruction from whatever cause by continuous gastric suction, fluid replacement, and the care of blood chemistry balance. The study and prevention of dehydration have been a major step forward. A surgeon of fifty years ago would rub his eyes in surprise at the changes that have happened here, for in his day everyone was immediately and incontinently operated upon, but with only moderate success.

Physiology has intervened in a most gratifying way in all branches of surgery, a point on which too much emphasis could not be laid. Most of the great advances in the treatment of thyroid diseases have a biochemical basis, and it is due to this as much as to increased practice in operating that all surgical treatment has been brought to so high a pitch of perfection.

Although Moynihan was the key figure in advances in abdominal surgery they were pressed forward by others who were not his actual disciples but had the same interests. At one time D'Arcy Power was a leader in London, surgeons coming to Bart's as pupils to see his gastro-enterostomies. There were Rutherford Morison and particularly Grey Turner in Newcastle-upon-Tyne; Arthur Burgess, Garnett Wright, Rayner, and of course John Morley in Manchester; Thelwall Thomas and Kelly in Liverpool; the Barlings and Sampson in Birmingham; James Sherren, that great man H. L. Barnard, Lockwood, Rowlands, Sir Percy Sargent, Sir James Walton, Zachary Cope, H. J. Paterson, and Pannett in London. The provincial surgeons concentrated on abdominal surgery more than the London surgeons, but it was perhaps a matter of opportunity above everything, since the provincial centres tended to place a much greater material in few hands. Very high technical skill tended to be greater in the provinces (so the provinces thought, probably rightly).

Outside Influences

British surgery being part of a confederation in a scientific sense, it would be wrong to omit mention of other schools of surgery. Europe had as great an influence on British surgery until the first world war as had America, and in the last century it had a much greater. It was the German politicians who destroyed German and Austrian surgery. No one can look at the family tree of Viennese surgery published in Schönbauer's book (*Das medizinische Wien*, 1947) without a feeling of wonder that so many great men should have come from the Billroth (1829–1894) stem. There were von Eiselsberg, von Hacker, Czerny, Wölfler, Mikulicz, Wagner, Sauerbruch, Clairmont, Ranzi, and now Denk and Schönbauer. Apart from these were von Bergmann, the chief proponent of asepsis, Bier, Volckmann, and, later, Küttner, Payr, and the elder Rehn. In Switzerland were the Reverdins and Roux, whilst Kocher in Berne had a great effect on British surgery, possibly the greatest of all in the 1900's, partly because of his own intrinsic merits, which were very great, and partly through the advocacy of Harold Stiles, who translated his great textbook. Kocher was surely a great man, an experimenter as well as a surgeon. In Brussels was Depage, in France there were the great figures of Doyen, of Henri Hartmann, Quènu, Jaboulay, Duret, Delorme, Delbet, of Theodore Tuffier (whom some considered the best-balanced surgeon in Europe). More lately there was the rise of the Scandinavians and Dutch, Einer Kay in Stockholm, with Schomacker and Noordenbos in Holland. All of these men made notable contributions to surgery, and many of them genuine innovations.

Of the Americans we remember W. W. Keen and especially Halsted with the Baltimore school that rose from him in a way reminiscent indeed of Billroth's, so that there was until recently scarcely a chair of surgery of any importance not held by a Halsted pupil, the most notable being Harvey Cushing. Besides there were the independents, J. B. Murphy, the Mayos, Howard Kelly, Hugh Hampton Young, and George Crile, not to mention others such as Jackson and Coffey, whose stars rose and fell with the now exploded mechanistic myths of visceroptosis, recalling the Curtis belt, that hall-mark of the psychoneurotic.

All these and many more whose names ought to be included not only wielded influence but greatly influenced one another not only through the increase of surgical journals but through international meetings and personal visits. On the whole the Continental leaders adhered to the doctrine of the all-importance of the professor who was polyvalent in all branches. Specialisms were little encouraged, because so many of the surgical chiefs of staff came to believe that it would be a serious loss of prestige if they admitted that someone else could handle a case better than themselves. Often they did not permit their juniors to have independent opinions or to discuss the foundations of their own. From these dreadful dogmas British surgery has been happily free: the worst that could be said about ourselves is that some seem to have had the ideal of performing like gifted amateurs at a difficult sport, as "gentlemen" rather than "players." One must admit that the idea has some charm, but at cricket it is the performer who gets out if he is rash. Undoubtedly our own age has seen the rise of the professional, a change made inevitable by the economic suppression of elegance (and a great pity that is) and also by the actual pressure of the work itself, which now leaves little time not only for fal-lals but also, and that most unhappily, too little opportunity for the general cultural self-education so necessary to happy existence and one that should continue throughout life.

It was always a mystery to the visitor to the Continent in the 1920's and 1930's that its knowledge of British surgery was so meagre. Continental surgeons were "insular" stay-at-home more than were we, so the sound common sense and sympathy with the patient's feelings and hopes that have always dominated British medicine were not seen by them at the bedside and were not appreciated. But it has always seemed to me that the British surgeon had not been able to get published the monographs on particular diseases or on important fragments that seemed to be so much more easily accomplished by his French and German and Scandinavian brothers. We have not yet found a way to remedy this defect, surely a serious one. We write many good textbooks for students, but the Continent no more reads those than we theirs (for that matter they are not so strong as we in that line). We have expanded our journals considerably, especially those that deal with special subjects.

The foundation of the *British Journal of Surgery* in 1913 under the most able editorship of Hey Groves, of grateful memory, was a notable event in the history of British surgery. It remains without a superior anywhere under Sir Cecil Wakeley. Equally the formation of the Association of Surgeons with the object of forming a meeting ground for all kinds of surgeons was a step forward, though it meets too rarely to exert as much influence as it might; whilst the reform of the Royal College of Surgeons, which Jonathan Hutchinson had called "a Golgotha of skulls," has somewhat dimmed its light. Reforms started by Moynihan but made really effective by the inspiration of Lord Webb-Johnson increasingly spread a beneficent influence, especially directed to the young entrant into surgery. It has added to its museums lively laboratories for active work. Another Moynihan creation and fine idea was the Empire Postgraduate Hospital at Hammersmith, where Grey Turner devoted his life to the new idea.

The Surgical Specialisms

The first war found the great surgical triumvirate by degrees in power—Moynihan, Sir Robert Jones, and Sir Harold Stiles. As their aids were Sir Anthony Bowlby, Sir George Makins, and Sir Cuthbert Wallace, with Sir Charles Ballance and Sir William Thorburn in the Mediterranean. It was from their collective work, helped by a select number of ardent and skilful young men who then and later made names for themselves, that the considerable advances in surgery mentioned above came. Abdominal surgery crystallized out whilst orthopaedic became once for all an established specialism. This was largely due to the inspiration of Sir Robert Jones, a truly remarkable figure, a modest man of vision and in fact of genius. His band of disciples—Sir Thomas Fairbank, Aitken, R. C. Elmslie, Sir Harry Platt, Rowley Bristow, Gaythorne Girdlestone, T. P. McMurray, and Naughton Dunn—created this division of surgery under Robert Jones's benign fatherhood. Biochemical advances and improved midwifery quickly made much of old-fashioned orthopaedic treatment unnecessary and instead canalized its activity into the treatment of industrial wounds and fractures, so important a service to the community.

Another great specialism already born for some years at the time of the first world war was neurosurgery, and in its advance suction and diathermy, new in the 1920's, had a great influence. But although its technical advances have been enormous in this half-century in the hands of A. A. McConnell, Sir Hugh Cairns, Norman Dott, and others in Britain, not to mention their elders, Sir Victor Horsley, Cushing, Frazier, Sir Percy Sargent, Dandy, Sachs, and the unique Wilfred Trotter, the chief change has been in mental outlook, in the growing contributions of the surgeons to neuro-physiology. Gone are the days of "barber-surgery" at the command of physicians, and instead a partnership exists. The same is true of thoracic surgery, the triumphs of which have been many lately in the public eye, with such ingenuities as the surgery of congenital malformation of the great vessels, thanks to the work of Blalock, Crafoord, Brock, Sellors, Bryce, Allison, and many more. And here must surely be paid a tribute to Morriston Davies as a world leader in thoracic surgery. His unlucky disablement at the height of his youthful powers restricted the magnitude of the contribution that he would have made, though not his influence. Surgery's grateful thanks should also go to the lamented Tudor Edwards, on whom the mantle of Davies descended, and most nobly he wore it.

Anaesthesia

That surgery owes a great debt to anaesthesia and the skill of the chemists in providing vast improvements is very plain. The change has been not only in the agents and technique of anaesthesia but in the discovery of hypnotic agents for the pre- and post-operative sedation. The abdominal surgeon of to-day must be grateful indeed for the advantages that curare gives him, whilst much of present-day intrathoracic surgery would be quite impossible were it not for the ingenuity and skill of the anaesthetists. The cumbersome pressure-changes of earlier years are

indeed gone with the wind. In neurosurgery it is the same story, but it is the same story everywhere. It is a pleasure to record the indebtedness of surgeons to the anaesthetist whose understanding and expert partnership have won him a new respect and importance. It is right and proper that much of what has happened should have been of British origin, because for at least two generations we have led the world in this vital matter.

No record of the time would be complete without mention of urology, dominated in its middle period by Thomson-Walker, that master of endoscopy like his follower Macalpine. The surgery of the prostate alone would call for a long chapter, with biochemistry again to the fore in the case of carcinoma, the development of the cold-punch technique, and Hey's championing of prostatectomy for retention—all most important advances. Similarly, no more than a bare mention can be made of plastic surgery, a subject in which Britain has for long been in the world leadership under the guidance of Sir Harold Gillies and his coadjutors, T. P. Kilner and Sir Archibald McIndoe. In surgical pathology the work of Sampson Handley on breast carcinoma and the me'anomas clarified the distinction between embolism and the process he named lymphatic permeation. This was an addition to knowledge of lasting value; comparable to it were the researches of Jamieson and Dobson on the visceral lymphatics. Nor should Sir Lenthal Cheatle's microscopy of chronic interstitial mastitis and Paget's disease be overlooked.

Conclusion

Looking back over the foregoing there have been a hundred omissions of men who deserve our gratitude and thanks, whose quiet and unassuming work has fortified and held the lines of communications of the more glamorous few. For although we cannot do without the adventurers it is the solid body who do the work, who accept the good and quietly discard the valueless. These men whose worth is often realized only by their near colleagues do invaluable services to mankind. But there are other names who clamour for more description of their work; Wilfred Trotter, who was the greatest intellect of them all, but will not fit into any scheme, has hidden himself somewhere. Perhaps his advocacy of the treatment of malignant disease in a rational way and not as a purely anatomical exercise in formal excisions would have most interested a Paget or a Hutchinson or a Billroth.

Nor has Victor Horsley's part as an experimenter and innovator been given sufficient place. Nor, again, is A. E. Barker here to whom we owed the development of local analgesia in this country, a debt indeed. And so, too, Butlin and Makins, Ernest Miles and Lockhart Mummery are not in the list, though they should have been, as should A. H. Tubby, the author of the most comprehensive work on orthopaedics in English. And what of Sir Thomas Dunhill, to whom we owed the modern operation of thyroidectomy and improvements in the management of thyrotoxicosis—and of Joll and Morley, who contributed so largely to this subject? And of Keynes's work on thymus and thyroid? Also omitted is the surgery of the sympathetic nervous system in which Stopford and Telford, Gask and Paterson Ross and James Learmonth pioneered; and not least in the surgery of malignant disease, in the developmental period of radiotherapeusis, the names of Sir Ernest Rock Carling and Sir Stanford Cade deserve gratitude not only for their technical skill but for their common sense in matters that call for the utmost in balanced judgment, a commodity that single-minded enthusiasts often lack.

It would not be out of place in this *Journal* for a surgeon to lay some stress on the part that the general practitioner has played in passing on to his patients the new benefits that surgery could afford them. It is often to him as much as to the surgeon that a patient's thanks should be given for his cure. But the practitioner himself had to learn, and we should not forget the great student teachers, Russell Howard at the London, Reginald Vick at Bart's, Mitchiner at St. Thomas's, Julian Taylor at U.C.H., and a score of others in London and the provinces who would as soon be remembered for this work as for their other contributions to surgery.

So brief a précis of all that has happened, of all the knowledge that has accrued by the labours of all those who have devoted their lives to the various branches of surgery, is almost derisory in its baldness. A life-time of active work and rich result has sometimes had to be recorded by a name, and by no means all of these could be cast into the framework of a sentence. But readers know to whom the palms should be awarded and they will pay in reflection their own silent homage to those to whom it should be made. But this brief chronicle is already in danger of stretching itself too far; a line must willy-nilly be drawn across the page.

FIFTY YEARS OF MIDWIFERY

BY

R. W. JOHNSTONE, C.B.E., M.D., F.R.C.S.Ed. F.R.C.O.G

Emeritus Professor of Midwifery and the Diseases of Women. University of Edinburgh; Consulting Obstetrician and Gynaecologist, Royal Infirmary, Edinburgh

No span of fifty years has seen such great advances in midwifery as the first half of the present century. The principal milestones are the birth and growth of the idea of antenatal care, the discovery of vital fresh knowledge about the aetiology of puerperal infection, the discovery of the sulphonamides and penicillin, the notable improvement in the methods and results of caesarean section, and the increased facilities for and better understanding of blood transfusion. The conquest of "puerperal fever," for centuries the scourge of childbirth, would alone justify my opening claim, for it has transformed the maternal mortality tables of the Registrars-General. From this and other causes the maternal mortality has been falling more rapidly than the general mortality, and it looks as if in a few years the death rate of pregnant women—admittedly a selected class—would be less than that of non-pregnant women in the same age group. But while this achievement has been the greatest and the most spectacular, the growth of the *idea* of antenatal care has been the most pervasive influence, and has worked the most widespread changes in the obstetrical outlook.

The Idea of Antenatal Care

At the beginning of this century any special care deliberately devoted to the object of preserving the health of the expectant mother, of treating any unhealthy conditions during pregnancy, and of foreseeing and, if possible, forestalling dangers likely to arise in her labour, so as to bring her and her baby safely through, was virtually unknown. In that admirable standard textbook of the period, W. S. Playfair's *Science and Practice of Midwifery* (1898), there are several chapters on disease in pregnancy, but two paragraphs, mainly concerned with the control

of constipation and the value of proper corsetry, are all that can be said to deal with the maintenance of normal health in pregnancy. There is no mention of antenatal examinations as such; no reference to the diagnosis of presentation and position by abdominal palpation either before or during labour; no suggestion of the pre-partum assessment of pelvic capacity in primigravidae, or even of routine testing of the urine for albumin and sugar.

As a result of this attitude of the medical mind the public mind showed a complete apathy on the subject and an ignorance of the "facts of life" (other than those immediately connected with impregnation) which was genteelly cloaked under the false modesty of convention. The young married woman when pregnant passed into "an interesting condition" not to be revealed even to the family doctor until a few weeks before his attendance was likely to be required, unless, indeed, gross symptoms such as vomiting, bleeding, or dropsy necessitated it.

Two sentences from Playfair exemplify what has just been said. "It is often sufficiently easy to recognize a pelvic presentation by abdominal examination *if we have occasion to make one*" (my italics). And again: "It rarely happens that deformities of the pelvis, except of the gravest kind, are suspected before labour has actually commenced, and therefore we are not often called upon to give an opinion as to the condition of the pelvis before delivery."

But the beginning of the century saw the dawn of the idea of preventive medicine, and when the new light fell upon obstetrics it ushered in the era of antenatal supervision. It was in Edinburgh that the new idea first germinated. Dr. Haig Ferguson at that time supervised the health of the inmates of a pre-maternity rescue home close to the old Royal Maternity Hospital. So impressed did he become with the normality of these girls' pregnancies and with the fine condition of their babies that he persuaded the hospital managers to offer similar supervision by means of an out-patient clinic to the married women proposing to come to the hospital for their delivery. To protect these respectable women from embarrassment, entrance to the clinic was arranged from an unfrequented side street, and I well remember the great consideration that had to be given to their modesty in putting up an unobtrusive and discreetly worded direction-board.

One of Haig Ferguson's colleagues on the hospital staff was J. W. Ballantyne, whose absorbing interest in foetal pathology had led him to wonder if anything could be done to prevent foetal abnormalities by treatment of the mother during pregnancy. He was persuaded to take over the management of this antenatal clinic—the first in this country—and in 1901 a bed in the hospital was endowed for the study of diseases of pregnancy—the forerunner of the antenatal wards of every modern maternity hospital. After some time Ballantyne recognized that the immediate value of antenatal care was much more in the interests of the mother than of the foetus, and, having grasped this truth, he very soon made himself the great apostle of the new gospel.

Teachers of midwifery hardly needed to be converted, so that the ultimate spread of the new doctrine was ensured, but it was greatly expedited by the shock to the national conscience caused by the deplorable revelations of national physique in the reports of the Ministry of National Service during and after the first world war. With unusual perspicacity it was recognized that the best place to start any reform was at the beginning, and that healthy babies required to have healthy mothers. Legislation permitting local authorities to establish antenatal clinics followed, and under the pressure of public opinion those of almost all the larger centres of population did so. As a result the organized practice of antenatal care may be said to have "got going" from the early 'twenties, and it is after that period that the national figures may be scrutinized for its effects. Nowadays there is a statutory obligation upon every practitioner undertaking maternity work that he will give at least the prescribed minimum of antenatal supervision to his patients, and it is estimated that in Britain about eight out of every ten expectant mothers do receive this measure of antenatal care, perfunctory though some of it would still appear to be.

In passing it is worthy of note that the same period, the early 'twenties, saw a nation-wide campaign started by the public health authorities against rickets, with the important incidental result that the frequency of contracted pelvis has been very greatly diminished amongst the young women who in these last ten years have become mothers.

A New Outlook

The results of antenatal care form an impressionist picture that must not be looked at from too near. To try to estimate the position by scrutiny of direct and detailed results is to get a wholly inadequate and disappointing impression. But if we stand well back and make a broad retrospective survey we realize that the great achievement of the teaching and practice of antenatal care has been to transform the whole outlook upon midwifery. It has made the medical profession "maternity-minded" to a degree hitherto unprecedented, with results that have pervaded every branch of clinical practice as well as the study of the basic medical sciences. One consequence of this in its turn has been that the lay mind has also developed a new and wholesome interest in maternity questions. The young married women of to-day respond with eagerness and intelligence to antenatal and mothercraft teaching. They demand a higher standard of obstetrical attention, and this has combined with the housing famine following two long wars to produce a very marked change-over in popular custom from domiciliary to hospital delivery, the potential results of which are far-reaching.

Regarded from this point of view, the influence of the idea of antenatal care has far exceeded the expectations of those who first cherished it. But while we consider this the most helpful viewpoint, let us not entirely disregard the details.

One line along which midwifery has been enormously improved by the antenatal idea is in the practice of the physical examination of the pregnant woman from both the medical and the obstetrical points of view. Abdominal palpation of the presentation and position of the child in the later weeks of pregnancy, investigation of the capacity of the pelvis—leading directly to the great modern contribution of the radiologist to accurate pelvimetry—the routine examination of the heart and lungs, the routine estimation of the arterial pressure, and the regular examination of the urine—all these are innovations of this century.

The almost religious attention that is now paid to the diet of the pregnant woman is an outcome of antenatal care which has been intensively fostered by the many years of compulsory national austerity. The results have been amazingly good, and dietetics is now our main hope in the prevention of abortions and premature births, and in the maintenance of healthy pregnancy generally.

Yet another far-reaching outcome of the antenatal idea is the increasingly great consideration now being given to

the life of the foetus in the choice and development of methods of delivery. Gone are the bad old days when dangers, unforeseen, had to be treated when and where they arose, and when consequently the obstetrician was often faced with a conflict between the interest of the mother and that of the child. As the preference had almost invariably to be given to the mother, the results to the child were often distressing, and it is gratifying to think that such a conflict rarely arises in good modern obstetrics. Examples of this modern trend are to be seen in the practice of external version in breech presentations recognized during pregnancy as well as in the general technique of breech deliveries; in the trial of labour with caesarean section in reserve in cases of moderate disproportion; and in the resort to the same operation in central placenta praevia.

How all this antenatal work shows up in the national statistics of maternal and infant mortality is a question to be approached with trepidation; so many possible factors are involved which are not obvious. The big facts are that in the years under consideration the maternal mortality rate has fallen to less than one-quarter of what it was and the infant mortality rate to about one-third. The maternal mortality figures showed no significant change until 1935, when a downward trend manifested itself, becoming precipitously steep in 1941. Analysis of the figures under the individual causes of death shows that puerperal and post-abortum sepsis, which used to be far and away the greatest factor, has now dropped to about one-sixteenth of what it was in the early 'thirties, and the rate for "toxaemias" (formerly the second greatest factor) to about one-quarter. Leaving sepsis out of account for the moment, this means that there has been a great diminution in the number of deaths due to hyperemesis gravidarum, pre-eclampsia, and eclampsia. Since there has been no great new development in the recent treatment of these diseases to which this rather sudden improvement could be attributed, it seems reasonable to give some of the credit to the progressive influence of antenatal care, although we ought not to overlook the possible but as yet unassessed effect of the increased vitamin B content of our "lower extraction" flour—one of the few and well-disguised blessings of the war. This distribution of the credit seems to be borne out by our own clinical experience that for ten years before the war severe hyperemesis was steadily diminishing, and that during the war it suddenly became practically an extinct disease, and has remained so. With regard to eclampsia, the improved figures strongly underline the value and importance of routine antenatal examinations; for the subjective symptoms of pre-eclampsia, so long as it is mild and comparatively amenable to treatment, are negligible, and only routine examinations will reveal them.

The Decline and Fall of Puerperal Sepsis

The dramatic drop in the maternal death rate from puerperal infection, which at the beginning of the century was as potent a lethal factor as all the other diseases and accidents of pregnancy and labour put together, has been mentioned. There seems no valid reason to doubt that we owe the "fall" of this dread scourge of womankind to the discovery of the su'phonamides and penicillin, but it was preceded by a "decline" for which obstetricians can take some credit. A quarter of a century's work in close association with bacteriologists had elucidated in great measure the aetiology of the disease. The principal organism was known to be the streptococcus, although on occasion a host of others could be found as well in infected lochia. It was generally accepted that much the commonest explanation of its presence was that it had been introduced into the birth canal from without—on imperfectly cleansed or contaminated hands, instruments, or dressings. The occasional presence of streptococci in the vagina prior to labour, although in a devitalized form owing to their inimical environment, was accepted as a conceivable but very rare explanation. Most of the responsibility therefore seemed to rest fairly and squarely on the attendants—doctors and midwives.

The next step was the classification of the various types or groups of streptococci by Lancefield and Hare, and the recognition that fatal cases were most often due to streptococci of Group A, less frequently of Group B. All this led to a tightening up of the aseptic and antiseptic technique of obstetric practice, but only a minor and disappointing degree of improvement ensued. The possibility of air-borne infection was therefore questioned, and when Smith, of Aberdeen, was able in no fewer than twelve cases to identify the streptococcus present in the lochia of women suffering from puerperal infection as precisely the same as that found in the nose or throat of one of their attendants (doctor, nurse, or student) the clue —"droplet" or "spray" infection—was in our hands. The wearing of sterilized masks over the mouth and nose became an important and integral part of our preventive technique, and we began to feel that we had at least gained some considerably increased control over infection.

Then almost before the full results of our preventive efforts could be assessed came Domagk's discovery of "prontosil," the clinical trials of which by Colebrook, under the aegis of the M.R.C., were extraordinarily successful. The sulphonamide era in therapeutics had begun, and its history is familiar. The conquest of puerperal fever had also begun, and the national statistics in due course began to show it. But the story was not yet ended. Whilst we were yet congratulating ourselves on the sulphonamides came the still stranger story of Fleming and Florey's discovery of penicillin, and the rout of this fell disease was soon complete. The position now is that a healthy woman, who has been kept fit throughout her pregnancy by intelligent antenatal supervision and delivered in decent circumstances with proper care and adequate precautions against infection, need have no fear of puerperal sepsis. And if, owing to some breach in technique, infection does occur, our powers of coping with it are immeasurably greater than they were fifty years ago.

The Haemorrhages

The figures of the Registrars-General reveal that in the last few years there has been a striking diminution in the number of fatalities from placenta praevia and a less noticeable improvement in regard to accidental haemorrhage. These facts may be taken to reflect recent changes in treatment, which may be summed up as (1) the transference of all cases of ante-partum haemorrhage to hospital where possible, and if possible without previous vaginal examination; (2) the avoidance of vaginal packing except where circumstances make it imperative as a temporary measure; (3) expectant treatment in hospital in suitable cases; (4) caesarean section in certain well-defined types of case; and (5) the replacement of lost blood by blood transfusion. Fifty years ago the maternal mortality rate in ante-partum haemorrhage ran at about 12% and the foetal rate at rather more than 50%. A general reduction in the maternal figures to about 6% with no corresponding improvement in the outlook for the chi'd was reached in many hospitals a few years ago. But Macafee showed in

1945 what could be done by concentrating the management of these cases under one person or a team working on a regular plan, by treating 174 cases of placenta praevia with a maternal death rate of 0.57% and a foetal death rate of 19%. For various reasons the foetal death rate in such cases will always be much higher than the maternal.

Post-partum haemorrhage, however, shows little sign yet of becoming a less menacing component of the maternal death rate, and this despite greatly increased facilities for blood transfusion. We have to remember that that remedy is itself not free from grave risk. But the wider adoption of the "flying-squad" system—whereby a selected team of doctors and nurses with obstetric skill and experience and familiar with the technique of blood transfusion can be sent at very short notice from a central maternity hospital to the patient's home, complete with all necessary equipment either to treat her there or more commonly to give her emergency treatment and then remove her to hospital by ambulance—would seem to be the best method of tackling this danger. We may reasonably hope to see better statistics on this point in a few years.

Operative Obstetrics

The most notable advance in this field has been in the methods and results of caesarean section. Apart from the increased safety given by the new chemotherapy and blood transfusion, the main source of this improvement has been the almost universal adoption of the lower-segment operation in place of the old upper-segment or "classical" operation. This bids fair to counteract the disconcerting frequency of rupture of the uterus in a subsequent pregnancy or labour which was the sequel of the wide employment of the older operation. In passing, it is interesting to recall that this method of incising the uterus was first suggested by Robert Wallace Johnson as long ago as 1769. We are not always as modern as we think.

The increasing recourse to caesarean section has meant a corresponding diminution in the use of the forceps in one field in particular in which the obstetricians of 1900 would have accorded that instrument the highest honours. I refer to contracted pelvis, or, more correctly, to cephalo-pelvic disproportion. The detection of pelvic contraction during pregnancy by antenatal examination, the more accurate assessment of the situation by radiography, and the adoption of the method of "trial labour" in appropriate cases, with caesarean section in reserve for cases in which the trial fails—all these have narrowed the scope of the forceps in this complication to a very small field. The "high" forceps operation has no place in modern obstetrics. "Axis traction" is now, therefore, of academic and historical interest rather than of living practical value. *Sic transit gloria.*

The Relief of Pain

It is just over a century since Sir James Young Simpson made history, as much by doing something previously undreamed of even by the most humane—namely, administering an anaesthetic (ether) for the relief of pain in childbirth—as by subsequently discovering that chloroform was a better drug for the same purpose. For fifty years and more doctors and their patients were content—and with very good reason, for chloroform, used as Simpson taught that it should be used, is still a first-rate anaesthetic towards the close of the second stage of labour. But the early years of this century saw the beginning of gropings after an analgesic suitable for use throughout the greater part of a labour, and "twilight sleep" with morphine and scopolamine was the first result. This was found to be not wholly safe for the infant, and in the last thirty years a great variety of sedative drugs, which seemed to pour out of the manufacturing chemists' laboratories in endless succession, have been tried with varying degrees of satisfaction. One of the last of these—pethidine—seems to have come to stay.

Public demand for some method of analgesia which could be safely administered by the midwife working without medical supervision led to the wide employment of nitrous oxide gas and air, but the necessary apparatus is too heavy for easy transport. "Trilene," which is free from that drawback, is now displacing it.

The importance of the control of the emotions and their bearing on the suffering experienced in labour has also been the subject of considerable study, and more is likely to be heard of this method of approach in the future.

Local analgesia by infiltration is widely and most beneficially practised during the period of distension of the pelvic floor and for immediate perineal repairs. Spinal analgesia is used by some in caesarean sections, and low spinal or caudal analgesia during vaginal delivery. Continuous caudal anaesthesia is more used in America than in this country.

Diabetes

Fifty years ago the diabetic woman rarely became pregnant, because the disease profoundly depressed ovarian function, and when she did so the prospect was gloomy in the extreme. One or even two out of every three such cases ended fatally, usually in coma, and the prospect of obtaining a living child was never more than about 50%. The discovery of insulin in 1921 completely transformed the scene. The number of diabetic women becoming pregnant is now quite considerable, and the maternal mortality in good hospital practice under the combined care of a physician and an obstetrician has been reduced to almost vanishing-point. For the child also the prospects are improved, although not to anything like the same extent. The undue size of these infants is a well-recognized factor of risk, but we do not yet know the reason for the intra-uterine deaths which often supervene in the last week or two of pregnancy.

Diagnostic Methods

The gaining of our new knowledge of the physiology of the female reproductive system has been one of the most dramatic happenings in the period under review, but for the most part it belongs to the sphere of gynaecology. It did, however, give obstetricians new biological methods of diagnosing early pregnancy with almost complete accuracy. The original Aschheim–Zondek test with mice was followed by the more rapid Friedman test in rabbits, and now the Xenopus toad holds the field. It is a more economical animal in that it gives its oracular answer by shedding its eggs and does not need to be killed and have its ovaries inspected.

Apart from pregnancy tests the use of the sex hormones in obstetrics has become limited by a process of trial and failure to the condition of missed abortion, in which very large doses of oestrogen seem to be helpful. Much was hoped, and even claimed, from the use of progesterone in the treatment of threatened abortion and more particularly in the prevention of "habitual" abortion, but extended trial has not fulfilled our hopes.

The diagnostic uses of radiography in obstetrics are so numerous that an *x*-ray plant is now an integral part of the equipment of any modern maternity hospital. In earliness of diagnosis radiography cannot, of course, compete with the hormonal tests, but in the second half of pregnancy it helps us in the diagnosis of foetal death, of

foetal structural abnormalities, of presentation and position, of plural pregnancy, of placenta praevia, hydramnios, and the like, as well as giving us methods of accurate assessment of the mother's pelvic capacity.

In this brief survey of the progress of midwifery I have had to avoid some attractive digressions into gynaecology, haematology (Rh factor), cardiology, foetal pathology (rubella in early pregnancy), and paediatrics. I have omitted any reference to the training of the medical student in midwifery, because it is too wide a topic, and to the training and control of midwives, because that falls under "Legislation." But there is one last achievement which must be mentioned, since it is not merely a milestone but a monument to the progress of obstetrics and gynaecology.

The Royal College of Obstetricians and Gynaecologists

In 1928 the British College of Obstetricians and Gynaecologists was founded, with William Blair Bell as its first president and William Fletcher Shaw as its first secretary. Broadly and briefly speaking, the establishment of the College was the natural and evolutionary outcome of the maturity of obstetrics and gynaecology as a conjoined branch of medicine. It signalized the blossoming of the branch, and we are now beginning to see the beneficial fruiting. The phenomenal success of the College in its first twenty-one years has been the best proof of how much it was needed in the interests of the two subjects not only in Britain but throughout the whole British Commonwealth. It has been singularly helped by royal favour, not only in the grant of a royal title and charter but in the active and generous personal interest of Her Majesty the Queen, who is an Honorary Fellow as well as Patron. Better proof of the "maternity-mindedness" of this generation could not be offered.

FIFTY YEARS OF MEDICAL RESEARCH AND PRACTICE

BY

Sir HENRY COHEN, M.D., F.R.C.P.

Professor of Medicine, University of Liverpool; Senior Physician, Royal Infirmary, Liverpool

"The art of progress is to preserve order amid change, and to preserve change amid order."—A. N. WHITEHEAD in *Process and Reality*.

"The last fifty years!" The phrase slips glibly off the tongue. Yet no era in the world's history has been so crowded with events of greater import for man or medicine. The twentieth century opened with Victoria still on the throne, and four monarchs were to succeed her. The conflict still raged in South Africa, and two wars were to follow and embroil the whole world. Each war was to overshadow its predecessor in ferocity, cruelty, tragedy, and destruction, until in the last it seemed that civilization itself might perish. Yet "out of evil came forth good," and medicine was enriched through the envies, bitterness, and follies of mankind. The third Marquess of Salisbury was Prime Minister; to-day his grandson is a notable figure in the House of Lords. The first underground electrical railway—the Central—opened in London in 1900; the first motor-bus and aeroplane, the first cinema and radio programme, and a host of other amenities and amusements without which it is to-day almost impossible for the vast majority of mankind to contemplate an acceptable life were still unknown. And legislation was to change, for good or evil, the social structure in every country in the world.

It is in this background and perspective that we must view the advances in medical knowledge and practice in the same period, for the history of medicine reflects the philosophy of its time. The dramatic discoveries in the basic sciences during this period gave to medicine its most potent instruments of research and tended to place the focus of medical advance in the laboratory rather than at the bedside, but the older methods which had their roots in the nineteenth century and even earlier were still to yield a rich harvest. For advance in knowledge is essentially evolutionary, not episodic; and no advance in clinical research leaves uninfluenced for long the practice of medicine.

Methods of Clinical Research

The methods by which clinical research and practice have progressed defy clear-cut enunciation. Few discoveries reach maturity without all known methods being employed, but in most can be discerned the motivating and predominant role of one of four methods. First, the recognition of clinical syndromes or recurring patterns of disease, commonly called "entities" or "diseases," and their investigation by all available techniques—pathological, biochemical, radiological, epidemiological, statistical, etc. When new techniques are developed they can be applied to earlier established syndromes and new knowledge gained. For example, the development of bacteriological techniques and their application led to the aetiology of many infectious diseases being revealed.

Secondly, experimental laboratory research has pointed the way to the interpretation of known clinical syndromes: from this, for example, we learnt to associate diabetes mellitus with the pancreas and diabetes insipidus with the hypothalamus.

Thirdly, there is the chance observation; the story of penicillin illustrates vividly the fact that though good fortune may attend discovery it comes only to the mind prepared for it.

And fourthly, there are the major discoveries in the cognate sciences—physics, chemistry, biology, psychology, and sociology—applied to the investigation of health and disease in the hope that these may yield some of their secrets.

It is of interest to trace in a few of the major advances in medicine in the last half-century the part played by these various methods, and the importance of perspicacious planning, a clear objective, concentrated effort, and team-work to clinical research.

Endocrinology

In few fields can the influence of these principles be better exemplified than in those of endocrinology and nutrition. Graves's disease, Addison's disease, myxoedema, and acromegaly had been described and their morbid anatomy was known before the century opened; and experimental excision of the adrenals had been shown to produce a fatal syndrome analogous to Addison's disease, and pancreatectomy a fatal glycosuria. But the science of endocrinology as we know it to-day is virtually a product of this century and begins with the discovery by Bayliss and Starling in 1902 of secretin, the first of the "hormones," or chemical messengers, which exerted a humoral as contrasted with a nervous control in the body. It was soon recognized by clinical observation and its correlation with pathological findings, by observing the effects of excision of glands both in the experimental animal and, in

rare instances, by operations on man, and by injection of their extracts or grafting transplants, that the pituitary, thyroid, parathyroids, suprarenals, pancreatic islet tissue, and gonads exercised a profound influence on such functions as growth and metabolism; whereas no hormonal function could with certainty be attributed to the pineal or the thymus, although thymectomy exerted a beneficial effect in many cases of myasthenia gravis.

But what is perhaps of greatest importance is that, during this century, study of the endocrines has led to a different orientation of medicine itself. The stress has shifted from alterations in structure in terms of morbid anatomy to disturbances of function in terms of morbid physiology. Since such disturbances could be in one of two directions—either excess or defect—clinicians sought to detect syndromes which could be interpreted in these terms. Thus tetany came to be recognized as an expression of parathyroid defect, and generalized osteitis fibrosa cystica one of parathyroid excess; the hyperglycaemia due to pancreatic islet deficiency was found to have its counterpart in hypoglycaemia due to overactivity of the islets. Where more than one type of cell entered into the composition of a gland, clinical research revealed syndromes associated with each type. The virilism of a suprarenal cortical adenoma was in striking contrast to the paroxysmal hypertension of the medullary chromaffinoma. The Cushing's syndrome of a pituitary basophil adenoma showed no superficial relationship to the gigantism and acromegaly of eosinophil overgrowth.

Indeed, we are to-day able readily to recognize most of the syndromes associated with excessive or defective secretion of the many endocrine glands and the various cells which comprise them; and where they are not yet recognizable we can prophesy, with the same confidence that the filling of gaps in the table of atomic numbers was foreseen, that sooner or later they will reveal themselves in the clinic.

The morbid anatomy of excessive activity of a gland may be a diffuse hyperplasia or hypertrophy, though more commonly a neoplasm, simple or malignant, is found arising from one type of cell, hence the specificity of the clinical pictures even in compound glands. But failure of growth or maldevelopment, and such destructive processes as inflammation, injury, degeneration, ischaemia, invading neoplasms, and the like, tend to destroy the whole gland. Hence, for example, although we recognize different syndromes related to neoplasms of the eosinophil and basophil cells of the pituitary, there is only one known syndrome of pituitary destruction—Simmonds's syndrome in the adult, and Lorain's syndrome in the child.

Thus during this century the concept of "diseases" as of "certain and determinate kinds" possessing "certain distinguishing signs which Nature has particularly affixed to every species" (Sydenham) has given way to the percept of "disease" as a disorder of function, accompanied by related structural changes, and brought about by many agencies, some necessary and specific, others predisposing, precipitating, and perpetuating.

The past fifty years in medicine has been marked by an increasing application of physico-chemical methods to the elucidation of disturbances of function in disease. For example, during the first twenty years of the century micromethods of blood analysis were perfected, and were applied, amongst others, to the study of endocrine disorders. Results of far-reaching significance in both diagnosis and treatment ensued. The disturbances in salt and water metabolism in Addison's disease and the place of salt in its treatment may be noted as a direct outcome of these studies, and it is doubtful if insulin or the parathyroid hormone would have been isolated if no method had been available for the estimation of the glucose or calcium of the blood.

The dramatic benefit which Murray had brought to the victims of myxoedema in 1891 by feeding them on extracts of sheep's thyroid—his article was published in the *British Medical Journal*—and the appreciation of the importance of hormones in the early part of this century, led to attempts to isolate other active extracts. Adrenaline in 1895, oxytocic pituitary extracts in 1909, the growth hormone of the anterior pituitary and insulin in 1921, oestrin and the gonadotropic hormone of the anterior pituitary in 1928, and the adrenal cortical hormone in 1929 are examples which not only filled a place in therapeutics as replacement remedies but were found to have other beneficial actions—e.g., adrenaline in asthma and pituitary extract in diabetes insipidus.

But these were relatively crude extracts, which provided a fertile field of action for the pure organic chemist. From many of these extracts were obtained pure crystals of biologically active substances. On Chrismas Day, 1914, Kendall isolated in crystalline form the thyroid hormone, thyroxine, so potent that it was estimated that 3½ gr. (0.23 g.) was the body's yearly requirement; in 1925 crystalline insulin was obtained, and in 1934 and later Kendall isolated a large number of crystalline hormones from the suprarenal cortex, all of similar structure, which included not only desoxycorticosterone acetate ("doca"), which plays an important though not exclusive part in the therapy of Addison's disease, but also "cortisone" or "compound E," which promises to revolutionize our treatment of arthritis and our understanding of the metabolism of connective tissue and immunity reactions.

The next stage was the determination of the constitution of these crystals and their laboratory synthesis. The structural formula for adrenaline was early revealed, but, although Kendall had isolated thyroxine in 1914, it was eleven years later that Harington showed it to be a derivative of tyrosine and assigned to it its proper structure, and a year after this that Barger synthesized it. As yet many hormones, including insulin, have defied synthesis, possibly because they have a protein structure, but some of the most complex have yielded their mystery to the skill and ingenuity of the organic chemist. And he has gone even further. It has been held, and there is much to support the view, that "Nature is still a cleverer chemist than man." Recent discoveries throw doubt on this assertion. Natural adrenaline is ineffective when given by mouth; the chemist has produced a synthetic adrenaline—isopropylnor-adrenaline—which is most potent orally. The natural oestrogens are complex cyclopenteno-phenanthrene derivatives and are of little effect when given by mouth. Dodds and others have synthesized artificial oestrogens of quite different and much simpler chemical configuration (alkylated derivatives of dihydroxystilbene). The general biological action of these is identical with the natural oestrogens, but they are active by mouth, can be of much greater potency with a more prolonged action, and are more cheaply prepared. The twentieth-century organic chemist may not have improved on Nature, but he knows a trick or two which are hidden from her.

There is a related study of which the last twenty-five years have revealed only the fringes, yet it may well be one of the most significant and rewarding in the years immediately ahead. It arises from three facts. First, that adrenal cortical hormones, including corticosterone and

compound E, the natural male and female hormones (androgens, oestrogens, and those of the corpus luteum), and methyl cholanthrene—a potent artificial carcinogen—have all as their characteristic ring system cyclopentenophenanthrene. Secondly, that oestrogens markedly inhibit the spread and growth of prostatic carcinoma, and to a less extent both oestrogens and androgens influence favourably the metastases of breast cancer. And thirdly, that cortisone seems to play an important part in the immunity reactions of the body. Are these three facts significantly related or is their association fortuitous? If the former, the solution of the problem of cancer and its control may be in sight.

Nutrition

Although the consequences of starvation and of fluid and salt restriction have long been recognized, and such syndromes as rickets, scurvy, beriberi, and pellagra known for centuries and associated with deficiency states, this century's contribution to research in human nutritional disorders has revolutionized our knowledge and transformed our practice. In this the study of vitamins and the part played by essential amino-acids are outstanding.

In 1885 Takaki showed conclusively the dietary origin of beriberi, and the measures he introduced led to its eradication from the Japanese Navy, where earlier it had been a serious problem. Over a century had then passed since Lind, by urging the issue of lemon juice, had performed a similar service which was to lead to the disappearance of scurvy from the British Navy. The early twenties of this century saw from Mellanby the first convincing evidence that rickets is a deficiency disease curable by a correct diet, and that the prevention of pellagra is through a proper diet.

The laboratory studies which were to reach fruition in this century began with Lunin's observation in 1881 that animals cannot live on a synthetic milk diet. In the last decade of the nineteenth century Eijkman had produced beriberi experimentally in fowls, the first time that a disease of dietary deficiency had been so produced, and he established that a diet of overmilled rice was the chief cause of beriberi.

But it was from Gowland Hopkins and his school that the major contributions were first to come, and within a few years there followed the isolation of individual vitamins, the recognition of the clinical and experimental lesions to which their deficiencies gave rise and of their modes of action, the determination of their chemical structures, and their large-scale manufacture. We now have the medical knowledge which, if applied, could virtually eliminate nutritional disorders. The planned rationing of the second world war, contrasted with the effects on the nutrition of the combatant nations of the first, is ample confirmation of this assertion. In the field of nutrition medical scientists have accomplished in great measure the tasks which confronted them. The next step lies with statesmen.

Haematology and Vitamin B_{12}

There is one chapter in the story of medical research which may profitably be summarized here, not only for its intrinsic importance but because it illustrates so strikingly the methods of clinical research in the past fifty years and the contributions made to it by workers in diverse scientific fields, each pursuing knowledge for its own sake.

Haematology has during this century been enriched by studies on the development of blood cells and their morphology, by the examination of haemopoietic tissues during life by marrow biopsy, by methods of blood chemistry and determinations of the physical properties of blood, by the application to the study of blood disease of genetics and immunology, and in a host of other ways. New clinical syndromes have been described, such as the anaemias associated with the names of Cooley and Lederer, and the Plummer–Vinson syndrome. Chlorosis, of which a lucid description had been given by Hoffmann over two centuries ago, and which was, to judge by the literature, a common disorder early in this century, was gradually to die out as the years advanced. The anaemias associated with iron deficiency were more clearly defined, and the need for adequate dosage of iron in their treatment was demonstrated. When the century opened the fifty-year-old problem of the essential nature and effective treatment of Addisonian (pernicious) anaemia remained unsolved. As the years passed it was increasingly recognized that it was not a disorder of blood-forming tissues only, but that the nervous and digestive systems were commonly affected. The neuropathies involved the peripheral nerves, the spinal cord, the optic nerves, and the cerebrum; glossitis and achlorhydria were signs of alimentary changes. Until twenty-five years ago treatment was confined to such measures as giving arsenic, hydrochloric acid, and blood transfusions, but life was rarely prolonged for more than a few years.

In 1925 Robscheit-Robbins and Whipple showed the beneficial effect of raw beef liver on blood regeneration in anaemia, and a year later followed the demonstration by Minot and Murphy of the specific effect of liver in pernicious anaemia. In 1929 Castle found that from the gastric mucosa could be obtained a substance active in the treatment of pernicious anaemia. Then came years of intensive research into the nature of the essential factor in liver. Although extracts of such potency that a few milligrams each month were adequate to maintain the patient with pernicious anaemia in good health, the pure active principle eluded isolation. Two facts contributed to this failure. The first was the difficulty of manipulating very small amounts of material for the processes of chemical separation; the second, the absence of a simple and rapid test for the haemopoietic activity of the isolated substances. The only subject for such a test was at that time the victim of the disease. The solution to both problems was to be culled from unexpected sources—the first from organic chemistry, the second from bacteriology.

The organic chemist in his investigations, especially on the isolation of plant pigments, had shown that when a mixture of these was passed down a specially prepared cylindrical filter, rings appeared at different levels at which the various constituents separated out (" partition chromatography "). Each of these rings could be removed and its content extracted. This made the separation of the different constituents of the liver extract a much simpler process. The bacteriologist had found that folic acid (one of the components of the vitamin-B complex) was an essential growth factor for *Lactobacillus lactis* (Dorner). Folic acid is an efficient haemopoietic agent in macrocytic anaemias though not an effective substitute for liver in pernicious anaemia; it fails to protect against the neural dystrophies in this disease. But it was shown that the antianaemic potency of liver extracts runs parallel to the growth requirements of the lactobacillus. This gave a simple and accurate method of rapid laboratory assay. By the application of these two discoveries in widely separated fields of science the isolation of vitamin B_{12} was made possible.

No topic could more vividly illustrate the lesson of the first half of this century that knowledge is an interlacing

network and that strands from many sources intermingle to give it fullness and strength.

Cardiology

The topics so far discussed have shown us a few of the notable contributions which during this century the chemist and biochemist have made to clinical research, and consequently to the practice of medicine. But the part played by the physicist has been no less noteworthy. Radiodiagnosis and radiotherapy, the construction of instruments designed to record the minute change in electrical potential accompanying activity in muscle, both voluntary and cardiac, brain, nerve, and even the retina, have led to results of great significance in our understanding of disease and in clinical diagnosis. All branches of medicine owe a debt to physics, but as an illustration of its contribution a brief survey of the evolution of our knowledge of heart disease during the present century is apt. A glance at the fourth edition of Osler's *Principles and Practice of Medicine* (1901), the most popular textbook of its day, suffices to reveal how little was then known. Most of the irregularities of the heart's rhythm remained undifferentiated and their significance was a sealed book.

Early in the century Mackenzie used in his general practice in Burnley a simple instrument, the polygraph, which recorded simultaneously the cardiac, venous, and arterial pulses. His genius enabled him by an analysis of these records to recognize the nature of most of the cardiac irregularities with which we are to-day so familiar, and long observation of patients led him to assess their significance and to differentiate those which could be ignored from those of grave import.

At the outset of the century Einthoven was perfecting the string galvanometer and was to show in 1903–4 how it could be applied to recording the electrical changes occurring in the human heart. In Lewis's hands this instrument was to reveal the mechanism of the heart beat and its disturbances in disease. Through him it was to become a diagnostic weapon without which no clinic was complete. In its development and use it was destined not only to illuminate disturbances of rhythm and conduction but also to throw light on the site and extent of coronary disease—one of the gathering enemies of mankind. Soon after, methods for recording the sounds of the heart and relating them to the electrocardiogram were devised.

What is sometimes forgotten, though it is of the utmost importance to the practice of medicine, is that the analysis and differentiation of, for example, the disturbances of rhythm revealed by these instrumental methods prompted the clinician to return to his patient and try to discover why the nature and import of these had earlier escaped him, and whether, with the additional knowledge gained through the instrument, he could now recognize by his own unaided observation what the instrument had revealed. He soon found that he was able to do so, and that he seldom needed the instrument to recognize extrasystoles and their type, auricular fibrillation, heart block, and the like, though in the difficult case instrumental help was still indispensable. With improvements in the techniques of physics other means of recording the electrical changes of heart and nerve have been introduced—e.g., the cathode-ray oscillograph.

The application of radiology to heart lesions revealed to the physician the pitfalls of his arts of percussion and auscultation, on which he had earlier relied. It made possible the recognition during life of such lesions as cardiac aneurysms. The injection of radio-opaque materials into the blood stream and observing the direction of flow and admixture of blood in the chambers of the heart (angiocardiography) have often made radiology the final arbiter in deciding, for example, the nature of a congenital cardiac lesion and its suitability for surgical repair.

As the years have passed, chemistry, especially the analysis of blood gases, has come to play an important part in the investigation of the problems of heart disease. Under radiological control, catheters can be passed through peripheral veins into the different cavities of the heart. The taking of samples of blood from these has helped to assess therapeutic measures in circulatory failure and to establish diagnosis, especially in malformations. These tests have often proved a necessary prelude to successful surgical intervention. The increasing contribution of surgery to the treatment of such lesions as patent ductus arteriosus and coarctation of the aorta demands accurate diagnosis. Surgery of the heart and lungs has been aided also by advances in antibiotic therapy, improvements in anaesthesia, and in measures for combating shock and blood loss. Investigations which have for their object the maintenance of an efficient cerebral circulation whilst the heart being operated upon is isolated from the circulatory mechanism are reaching a stage at which success seems in sight.

The introduction by Riva-Rocci of the mercury sphygmomanometer in 1896 led during the ensuing years to increasing interest in the significance and mechanism of high blood pressure. Few clinical problems have been so extensively investigated in the past fifty years, but, though much light has been shed on certain forms of hypertension by laboratory and bedside studies, knowledge of its intrinsic nature and its effective management still remains meagre.

The application of physical instruments of great precision has not been confined to cardiological practice. The electroencephalograph, following on Berger's discovery in 1929 that action currents of brain activity can be registered, has opened new fields of investigation in the epilepsies and in the localization of cerebral lesions, and the electromyograph is helping increasingly in the diagnosis of muscular lesions. Moreover, improvements in lenses and in lighting have led to the devising of instruments which make it possible to see into the cavities of the body. The sigmoidoscope, cystoscope, oesophagoscope, gastroscope, bronchoscope, the electrical ophthalmoscope and laryngoscope, and many other ingenious instruments have been constructed, and cameras for permanent recording attached. The electron microscope has opened new fields of research into the ultramicroscopic world, especially of viruses.

Radioactivity

The immense significance to medicine of Röntgen's discovery of *x* rays in 1895 was immediately recognized, and within a year or two it was applied to the diagnosis of bone disease and injury, stones in the urinary tract, foreign bodies, and similar lesions. With improvements in technique the softer tissues—e.g., the lungs and kidneys—were later visualized in sufficient detail to be of considerable help in diagnosis, and as the years have passed in this century the ingenious use of contrast media—e.g., barium in the alimentary tract, lipiodol in the bronchi and spinal theca, air in the cranium and peritoneum, iodine derivatives in genito-urinary and biliary tracts, the circulation, etc.—have made *x*-ray examination an almost indispensable contribution to accurate diagnosis in innumerable diseases.

Becquerel's chance observation of the destructive effects of radium, which the Curies had isolated in 1898, although

following the earliest use of *x* rays in treatment, was the starting-point of the science of radiotherapy, which has seen such strides in the past few decades.

But what could not have been foreseen was the gift to medical research which fundamental investigations into the structure of the atom was later to yield through the genius of Thomson, Rutherford, and their co-workers, especially Chadwick and Aston. In 1934 came the outstanding discovery of Curie and Joliot, that ordinary elements which are found in nature in the stable state can be induced to become radioactive. Investigators thus had at their disposal atoms of a wide variety of elements of biological interest, which by means of special recording instruments could be easily traced by their radioactivity. Thus a method became available for following "labelled" atoms in the myriads of complicated reactions which occur in the body, both in health and in disease, and also for delivering radiation treatment direct through the blood stream to the various tissues of the body. A few examples will suffice to illustrate the uses to which these radioactive isotopes have been applied.

Radioactive iodine (I^{131}) has been used in studying the physiology of the thyroid, in the recognition of thyroid disease, in the location of brain tumours with diiodofluorescein, and in the treatment of hyperthyroidism and thyroid carcinoma. Radioactive phosphorus (P^{32}) has found a special place in the study and treatment of blood dyscrasias—polycythaemia, leukaemia, lymphosarcoma, and myeloma; in metabolic investigations on nucleo-proteins and phospho-lipoid synthesis; in the elucidation of the malaria-plasmodium-host relationship; on the vascular capacity of heart and kidney; and on the fate of labelled antigens and rate of antibody production. Radioactive calcium (Ca^{45}) has made significant contributions to our knowledge of bone growth, and radioactive sulphur (S^{35}) to the role of sulphur-containing amino-acids in protein metabolism. The life story of the red blood cell has been illuminated by radioactive iron (Fe^{59}), and a wide variety of uses in medical research are being made of radioactive carbon (C^{14}), sodium (Na^{24}), potassium (K^{42}), and other elements. This is yet an infant field, but few infants have shown greater promise of vigorous growth.

Infectious Diseases and Allergy

The last three decades of the nineteenth century had seen rapid strides in our knowledge of the infective agents in disease. Among bacteria had been described staphylococci, streptococci, pneumococci, meningococci, and gonococci; the bacilli of typhoid, tubercle, leprosy, glanders, tetanus, undulant fever, diphtheria, plague, dysentery, and gas gangrene; the malaria parasite and the entamoeba of dysentery; and fungi of actinomycosis and sporotrichosis. The role of vectors, especially in tropical diseases, was well established. The first twenty years of the twentieth century saw an intensive development of bacteriology and protozoology and the recognition, using special media and techniques, of tens of thousands of organisms of which only a small proportion could be regarded as responsible for disease. Many new diseases, including tularaemia, histoplasmosis, toxoplasmosis, melioidosis, and others were recognized.

The phenomenon of bacterial agglutination, discovered in 1896, had been rapidly followed by its application to the diagnosis of typhoid, and later to dysentery, brucellosis, and other infections. Clinical pictures superficially similar, as, for example, the enteric fevers, were found to be due to organisms which differed in their cultural characteristics, their fermentative properties, and their agglutinins. The many types of paratyphoid, dysentery, and food-poisoning infections were differentiated. In 1901 the phenomenon of complement-fixation had been discovered, and five years later, and just one year after the *Treponema pallidum* had been revealed as the causative organism of syphilis, came the Wassermann reaction. Later the complement-fixation test was applied to other diseases. Vaccines, antisera, and antitoxins were soon to follow, and then came prophylactic immunization in diphtheria and whooping-cough, which was to have so great an effect on infant mortality from these diseases and to give promise of similar success in tuberculosis by the B.C.G. vaccine.

The production of antibodies in the blood of infected patients, however, was not only to lead to these mighty therapeutic advances but was also to throw light on a group of diseases of which but little was earlier known. Before 1890 there were scattered observations in the literature suggesting that certain cases of asthma were caused by the inhalation of dusts, pollens, and dandruff, that urticaria and "gout" occasionally resulted from an idiosyncrasy to food, and that eczema might follow on contact with certain plants. But it was the reactions from diphtheria antitoxin—serum shock, serum disease, and anaphylaxis—that led to the conception of allergy as a tissue sensitization, inherent or acquired. This was to have an important influence on the interpretation of disease in this century. Advances in these directions have almost transformed the taxonomic bacteriologist of the earlier part of the century into the immunochemist of to-day, and advances in chemotherapy have revolutionized, as Sir Henry Dale so vividly relates, the treatment of infectious disease.

Many diseases were from their clinical characteristics suspected of having a bacterial origin, yet the methods in use failed to reveal it. This century has seen the isolation and significance of two further groups of pathogenic organisms—the rickettsiae and the viruses. The rickettsiae are minute bacteria causing, for example, typhus, but they are of little interest in this country. It is just fifty years since a virus was established as the infectious agent of tobacco mosaic disease; in a decade or two, yellow fever, rabies, vaccinia, variola, and poliomyelitis were identified as of virus origin; and to-day, with similar methods of isolation being used, there is reason to suspect that herpes zoster and febrilis, varicella, psittacosis, influenza, many forms of encephalitis, warts, and molluscum contagiosum, amongst other infections, are due to viruses.

In the earlier part of the century we see in retrospect an undue emphasis on the role of living organisms in the causation of disease. This was an understandable response to the isolation of a specific cause and the rigid application of Occam's razor—"Entities should not be multiplied beyond necessity." But as the years passed it came to be recognized more widely that the organism, though a necessary agent, is rarely sufficient of itself to produce disease; that constitutional bias, the nutritional state, occupation, exposure, and a host of physical and chemical factors play a part in all infections; and that the manifestations of the disease are modified by all these factors. It is indeed the appreciation of these predisposing and perpetuating causes of disease that has led in the past twenty years to the emergence of "social medicine" as a separate discipline

Neurology

The help given to neurological research and diagnosis by radiology, especially pneumoencephalography and arteriography, and by electrophysiology has been earlier

acknowledged. It is in this province also that clinico-pathological correlation, the main instrument of medical research in the late eighteenth and nineteenth centuries, has continued in this century to make valuable contributions. The recognition of many new syndromes—e.g., Wilson's disease—has thrown light on the functions of the basal ganglia and the related subthalamic nuclei, and to this study the epidemic of encephalitis and its after-effects from 1917 onwards gave fresh impetus. The first world war provided the opportunities which led to the classical work by Gordon Holmes on injuries to the visual cortex and cerebellum and, with Head, on sensory pathways and aphasia. Sherrington's fundamental work in neurophysiology, especially on reflexes, tonus, and integrative mechanisms in the nervous system, was to find important applications in neurological practice. Many new reflexes were to be described on the basis of necropsy findings—e.g., the extensor plantar response in pyramidal disease. The work of Golgi and Ramón y Cajal on neurohistology was to be extended: one of its fruits was the monograph by Bailey and Cushing on gliomas—a classical example of the fertile collaboration of clinician and pathologist

In the past thirty years the neurosurgeon has been able to add to our knowledge, especially on cerebral localization and epilepsy, by direct observations, on man, of the effects of stimulation of the exposed brain.

In this context it is proper to refer to the growing recognition of the part played by psychogenic factors in disease associated with structural change—e.g., in peptic ulcer and allergic states. In recent years this has led to a concept of psychosomatic medicine which has re-emphasized the absurdity of body-mind dichotomy.

Conclusion

The tests which have been devised to assess the functional efficiency of most of the organs and tissues of the body and the use made of these in diagnosis and in the control of treatment; the major advances in therapy, both medical and surgical, especially in recent years; the achievements of preventive medicine; and many other topics which are the subjects of separate contributions to this symposium testify to advances in practically every branch of medicine no less serviceable to mankind than those here reviewed.

But the story must not be thought of as one of unimpeded and triumphal progress nor narrated wholly in the jubilant terms of victory. For the mastery of many diseases still evades our grasp and most conquests have brought forth fresh problems. The treatment of cancer is still based on a primitive and barbaric interpretation of the injunction, "If thy right hand offend thee cut it off," though recent years have given hints of deeper understanding. The expectation of life has risen in the past half-century by about fifteen years. Yet increasing longevity has its hazards in the greater incidence of cancer and degenerative disease of the heart, blood vessels, and brain.

The obstacles to be surmounted in the control of disease are still many, but, with the experience of the first half of the twentieth century in mind, he would be a bold prophet who would venture to predict the limits of future achievement. More heights will be scaled, and on their summits may be firmly planted the emblems of progress; but some will reveal that the topmost heights are not yet reached. To conquer these, wisdom will bid us recall the one lesson above all others which the story of "combined operations" here related teaches—namely, that every branch of knowledge has its contribution to make to the goal of medicine, and that this goal is not only the prevention and cure of disease but also the raising of standards of individual and community health, taking as its motto the words of Martial: *Non est vivere, sed valere vita est*—Life is not living, but living in health.

FIFTY YEARS OF CLINICAL PATHOLOGY

BY

Sir LIONEL WHITBY, C.V.O., *M.C.*, M.D. F.R.C.P.

Regius Professor of Physic, University of Cambridge

The title of this article naturally raises the question of what is meant by clinical pathology. When does pathology become clinical, as distinct from an academic pure science several stages removed from everyday medicine, and when does clinical work become inseparably associated with procedures which can be performed only in a laboratory, rather than at the bedside? One might define clinical work in simple terms as that work which can be performed at the bedside. But it is impossible to separate this work from pathology, in that the clinician is observing and pronouncing his opinion upon pathological processes many of which are susceptible of laboratory investigation and control. The evolution of clinical medicine was gradual, whilst the impingement of the laboratory upon the bedside has become ever more prominent in the past fifty years in parallel with the geometrically progressive speed of scientific advance.

At the close of the nineteenth century the practice of clinical medicine had reached a remarkably high standard. Those were the days of the great individualist, of the outstanding man who, with no more equipment than his five senses, his experience, a few crude instruments and rough side-room tests, his wits and his instinct, would make a shrewd and remarkably accurate assessment for prognosis and diagnosis, though treatment was limited by lack of knowledge of primary cause or of specific measures. There were no exact checks upon the accuracy of the opinion apart from the final assessment in the post-mortem room. Be it said to their credit that most clinicians of the period, though opinionated and dogmatic at the bedside, more often than not with full justification, nevertheless regularly checked their opinion in the post-mortem room, thereby deriving experience and knowledge from their mistakes. They frequently performed the post-mortem examinations themselves, and usually conducted lectures and taught the pathology and morbid anatomy of disease—work which nowadays is carried out by a department of pathology.

These masters of the bedside art combined their clinical work with the practical pathology of their hospitals; they were well versed in morbid anatomy and in the limited tests for physiological functions which were then known. Their views, their teachings, their wisdom, and their technique spilled over into the twentieth century, so that many whose age is parallel with or in advance of the years of the century are greatly indebted to them for a clinical teaching the excellence of which is never likely to be seen again. Nowadays the tempo of life is so fast, the demand for medical treatment so large, the detail of every specialty so great, and the complexity of scientific checks and treatment so vast that no one man could achieve such general excellence and with such unhurried or courtly confidence as the masters of the past.

Meanwhile, behind the foreground of the clinical perfection of the nineteenth century the science of pathology,

which included bacteriology, immunology, histology, morbid anatomy, and the early phases of haematology and chemical pathology, grew apace and began to extend into clinical medicine by reason of practical applications.

Bacteriology

Pasteur, Koch, and others had established the bacterial nature of many diseases. Hence it was often possible to prove a causal factor by successful demonstration of the specific organism in smear or culture of appropriate material. Immunological studies had established the specificity of antibodies and had shown the virtues of at least one specific antitoxic serum—for diphtheria. Hence a bacteriological check could confirm the necessity for diphtheria antitoxin or could go some way towards identifying the likely candidates for antitoxin treatment before clinical signs had appeared. Furthermore, certain of the phenomena associated with immunity—agglutination, precipitation—were seen to be applicable to the diagnosis of active disease. Grüber and Durham in 1896 had shown that the serum of patients suffering from typhoid fever would agglutinate the typhoid bacilli, while Widal and Sicard in the same year extended the discovery to show that a patient's serum could be tested with bacteria of known type for the purpose of identifying disease. This principle, which is often called Widal's reaction, should rightly be called the Grüber–Widal reaction.

Bacteriology and immunology were in fact the first of the laboratory sciences to make any considerable intrusion into bedside medicine, and in the early phases these sciences demanded no more than an appropriate sample of a body fluid, a secretion or an excretion, which could be competently examined. For example, in 1901 Bordet and Gengou had established the principles of the complement-fixation reaction, which Wassermann, Neisser, and Bruck extended in 1906 as a specific test for syphilis soon after Schaudinn and Hoffmann in 1905 had demonstrated the spirochaete and Levaditi (1906) had stained it. In 1904 Almroth Wright and Stewart Douglas announced their work concerning the presence of opsonins in immune serum. Later they introduced to medical practice the view that the autogenous vaccine, carefully administered with frequent tests for opsonin control, would be the solution to all problems of disease or disability arising from acute, subacute, or chronic bacterial infections. This phase of bacteriological work may be seen in perspective as the beginning of a period when the pathologist was required to give personal attendance to the patient in order to study his general condition as well as the properties of his body fluids. This period, which may be called the "vaccine era," had an innings of about a quarter of a century, until accumulated experience had shown that such therapy had not the value in everyday medicine which its originators, with all honesty of mind, had anticipated.

In 1908 Bela Schick introduced the dermal test for susceptibility to diphtheria. Then there were the various tuberculin sensitivity tests of von Pirquet (1907) and Mantoux (1910). In 1924 the Dicks announced their test for determining individual susceptibility to scarlet fever. The carrying out of these tests was originally the function of a clinical pathologist, but wide application and constant practice have now made such tests an everyday procedure which can be performed by any doctor who acquires the small amount of skill necessary to make a neat intradermal injection. The natural corollary of these tests for susceptibility was the development of measures for the control of epidemic and infectious diseases, including the devising of methods for immunization as well as for dealing with the problem of "carriers" and the control of epidemics. Advances in this field have had the effect of returning much of the bacteriological work of the clinical pathologist from the patient—a position demanded by the vaccine era—to a fully equipped laboratory where the exact and intricate procedures associated with epidemiological problems can be impersonally performed.

Thus the work of Rebecca Lancefield (1933) in differentiating haemolytic streptococci by serological methods, the publications of Felix and Pitt (1934) on the antigens of *Bact. typhosum*, the development of phage-typing, the devising of selective culture media, and other purely laboratory devices have meant that the work can be efficiently and economically performed only in centralized laboratories which hold stocks of the multiple and sometimes rare sera, and all the other necessary paraphernalia. The stimulus for the creation of central laboratories was given by the 1939–45 war, and the organization then set up has been incorporated into the National Health Service as the Public Health Laboratory service, which is equipped to deal with all bacteriological and epidemiological problems, as well as the serology of infectious diseases.

Chemical Pathology

With chemical pathology the story has been different. This branch of clinical pathology has at the present time come to form a very large part of the specialists' work. At the turn of the century the subject had reached the side-room stage, mainly with qualitative tests for urinary abnormalities, whilst Ewald, Boas, and Einhorn, in the last decade of the nineteenth century, had devised crude methods for investigating gastric function. These, however, were not generally practised until Rehfuss in 1914 advocated the fractional test-meal, the potentialities of which were exploited by the Guy's school in the years after the 1914–18 war, by Hurst, Ryle, Izod Bennett, Baird, and others, who perfected the technique of gastric analysis, indicated the scope as well as the limitations of the test, and introduced the important practice of histamine administration.

In contrast, the correlation of blood chemistry with excretory chemistry had almost no foundations in the nineteenth century. To Abderhalden, van Slyke, Folin, Wu, Stanley Benedict, and others we owe the development of blood chemistry, after the practice of venepuncture had come to be regarded as commonplace and following upon the perfection of colorimetric methods of estimation. Carbohydrate metabolism has always lent itself to chemical methods of investigation. Hugh MacLean's micromethods for blood analysis and his technique for sugar tolerance, published in 1921 in collaboration with de Wesselow, can be regarded as landmarks—likewise van Slyke's methods for detecting acidosis, published from 1917 to 1919, as well as his methods for investigating renal function such as the urea-clearance test. General metabolic investigations had begun in the 'nineties with the work of Atwater, with whom Francis Benedict worked, so that the latter came to publish the first practical method for estimating basal metabolism in 1918.

But the event which inevitably brought the chemical pathologist to the bedside was the discovery of insulin by Banting, Best, and J. J. R. Macleod in 1922. The more complete understanding of carbohydrate metabolism and the significance of glycosuria which previous work established had to be fully exploited in order to be sure of an accurate diagnosis before using a specific remedy which could be as lethal in wrong dosage or when wrongly applied

as it could be curative when properly used. Each diabetic came therefore to need individual investigation for purposes of stabilization and control and for the ordering of the rest of his life. Under modern hospital conditions much of this control can be impersonal so far as laboratory examinations are concerned, but in the smaller districts such work has generally come into the hands of the local clinical pathologist—likewise with the investigation of cerebrospinal fluid, renal function, liver function, gastric function, fat metabolism and balance, basal metabolism, and the various enzymatic changes that have been found to be associated with malignant or other changes in particular organs, as well as the complex problems of coagulation of the blood which involve many chemical procedures.

This subject, then, has made vast strides in the first half of the century, and, since the basis of all physiological function must be chemical change, it can be anticipated that the chemical pathologist will play a greater and greater part in the future in the diagnosis, control, and cure of somatic disease.

Morbid Histology

Morbid histology, being a branch of pathology which lends itself to academic laboratory study, had naturally developed to a considerable degree in the nineteenth century following upon improvements in the construction of the microscope, in methods for section-cutting, and in the development of differential and specific staining. During the past fifty years this aspect of pathology has come to have a more immediate application at the bedside or in the operating theatre, in that the scope of surgical intervention can be greatly influenced by the nature of a pathological process, whilst exact diagnosis often depends upon the histology of a biopsy specimen. Furthermore, there is now a clearer appreciation of the fact that specific and differential staining is entirely a function of the chemical composition of the tissue which selects the differential stain. This has opened up the subject as a means of studying the chemical physiology and pathology of the body tissues.

Much of morbid histology is concerned with the diagnosis of malignant disease, which, in the present state of knowledge, has a prognosis largely governed by surgical intervention at an early and operable stage. Hence the morbid histologist is in frequent demand for a rapid diagnosis and for general biopsy work. This, in great centres, is largely concentrated in separate departments, but in country districts the task falls to the lot of the general clinical pathologist and may occupy a great deal of his time. The work requires considerable experience, such as may be acquired only by long training in a big institution. With such training a correct opinion demands little more than a quick examination in some 90% of the work. The remaining 10%, the unknown quantity, may remain unsolved, with conflicting expert opinions, until the course of nature has revealed the true significance of the pathological changes.

Haematology

At the beginning of the century the science of haematology had begun to evolve. Methods were available for a simple and relatively accurate determination of haemoglobin (Gowers, Haldane) and for the enumeration of red cells and leucocytes, whilst Ehrlich's triacid stain (published 1877), which had first differentiated the granular cells of the blood and led to the technique of the differential count, was coming to be replaced by the eosin-methylene-blue combinations, of which the first—Romanowsky's stain—was described in 1891, followed by the well-known Leishman stain in 1901. But in those days haematology was simple. The frankly leukaemic forms of the myelogenous and lymphocytic varieties of leukaemia could be recognized. The anaemias were regarded simply as primary or secondary, according to whether the cause (often haemorrhage) was known or not, whilst pernicious anaemia, then classed as primary, was identified by the high colour index and by the gross corpuscular abnormalities of the terminal stages which are never seen to-day.

Even in a general hospital the performance of a blood count was something of an event; it was done by a pathologist who usually had little interest in the clinical aspect and whose facts and figures served the physician to orientate the case as primary or secondary. Through the fifty years of this century there has been a vast accumulation of knowledge concerning the blood changes which may be associated with almost every disease, so that a blood count has come to be almost a routine, especially in patients in whom the diagnosis is not clear or in whom progress has to be watched. The value of a competent and complete morphological examination of the peripheral blood has been established by the work of such men as Naegeli, Schilling, and Arneth. Many events have arisen which have gone to make haematology almost a separate science, notably the multiplicity of techniques. The perfection of these has shown, for example, the significance which may be attached to a close examination of the dimensions of the red cells, the intricacies of haemoglobin metabolism, and such non-specific features as the sedimentation rate—itself often performed as a side-room examination. The development of knowledge concerning coagulation has increased the field of essential control tests in both medical and surgical disease.

The skill and constant practice required to carry out the time-consuming procedures neatly, accurately, and precisely are beyond the compass of the general physician, whilst the best interpretation of results is possible only to those who have a full knowledge of the clinical aspects of disease and who are steeped in the ever-changing literature of the subject. The haematologist must also be aware of the many extraneous conditions which may lead to minor and even major alterations in a blood picture, and most of these can be ascertained only at the bedside. Certain it is that a blood examination badly or inaccurately performed is more of a menace than a help, whilst if the result is interpreted without due care the deductions may be dangerously misleading.

As with chemical pathology, so with haematology. The outstanding therapeutic discovery by Minot and Murphy, announced in 1926, of the curative effect of liver in pernicious anaemia translated haematology from being an interesting laboratory subject to being a bedside procedure for the accurate diagnosis of pernicious anaemia and for the exercising of exact scientific control upon the effects of treatment. No physician can now be satisfied with the cure and maintenance of a case of pernicious anaemia without supporting evidence from his clinical pathologist. And this has shown that there are wheels within wheels, that though all cases of pernicious anaemia exhibit a megalocytosis, not all those which exhibit megalocytosis have pernicious anaemia. The diagnosis and treatment of such cases present intriguing and fascinating problems which only the expert clinical haematologist, in the closest association with his clinical colleague, can successfully solve. Bedside haematological control is now an

essential part of treatment involving any of the drugs known to have a toxic haemopoietic effect, whilst the constant watch which has to be kept on all who are exposed to irradiation hazards has, in these days of atomic energy, led to an enormous demand for skilled clinical haematologists.

One more stone, albeit an important one, in this edifice of co-operative clinico-pathological work was added when Arinkin in 1929 outlined the possibilities associated with an examination of the marrow from samples obtained by the simple operation of sternal puncture. Before that time the study of blood disorders had been confined almost entirely to samples of the peripheral blood supplemented sometimes by an examination of the marrow at necropsy, by which time degenerative autolytic changes have occurred which obscured the essential features required for fine structural differentiation. It has been said that in earlier days the great haematologist Wilhelm Türk (1871–1916), when asked to comment upon bone-marrow findings as compared with the results obtained from a blood examination, observed, "Sir, I am a peripheral haematologist." Now, in 1950, a marrow examination is regarded as a commonplace, whilst an expert opinion upon the cytology and architecture of the marrow is an essential procedure in many anaemias, as well as in obscure bony lesions. The analysis of the cytology of such samples calls for expert opinion, which in turn must be closely correlated with both the peripheral blood and the clinical findings in all cases when the result is not diagnostic.

In 1900 Landsteiner divided human blood into three groups according to the iso-agglutinin content, whilst his pupils, Decastello and Sturli, added the fourth group in 1902. It was not, however, until 1910, when Moss's paper gave wider publicity to this important matter, that blood transfusion began to be practised, making its real entry into everyday medicine as the result of experience in the 1914–18 war. Faith in this simple Landsteiner classification endured for almost thirty years, but was rudely shattered by the implications arising from the discovery and investigation of the Rhesus factors by Wiener, Peters, Landsteiner, Levine, Taylor, Race, Fisher, and others from 1940 onwards. In the past decade the development of what is now known as immunohaematology, in itself almost a subdivision of the main subject, has made the art of blood transfusion so complicated a procedure and has imposed so many scientific controls and investigations in pregnancy, in haemolytic anaemias, diseases of newborn infants, and in cases of multiple transfusion that only a handful of experts aided by geneticists can understand all the ramifications. The everyday control of such matters and the essentially practical aspects are the functions of the clinical pathologist in close association with the National Transfusion Service, which has a centre in every Region.

The Clinical Pathologist

An interesting aspect of clinical pathology, among all this welter of scientific advance, has been the evolution of the clinical pathologist himself, especially his eventual establishment within the practising profession as an essential figure in consultant and specialist work. The development of status has been different according to whether the clinical pathologist has been attached to a large teaching hospital or has been a member of the staff of one of the many non-teaching hospitals which serve such large sections of the population throughout the country.

At the beginning of the century and for upwards of twenty years the pathological department of even a teaching hospital was on the whole poorly equipped, whilst the posts were usually ill paid; much of the revenue had to be derived from the rewards for hack work which the department performed. The clinico-pathological section formed but a small part of the main department, which itself was largely concerned with academic work, teaching, post-mortem examinations, and morbid histology. The routine bacteriology, haematology, and biochemistry from 1900 to 1910 at first required a staff of no more than one or two, assisted by a technician. Such men rarely penetrated to the wards, save for the collection of a specimen. Their work was mainly bacteriological owing to the rapid advances that had been made in this subject during the eighteenth century; their status was low even in their own department. Even as late as 1920, with all the extension of clinical pathology that had arisen from the experience of the 1914–18 war, it was not uncommon for most of the work to be concerned with samples of excreta brought to the laboratory, sometimes through a hatch, by the clerks and dressers of the clinical firms. From 1918 onwards the importance of clinical pathology grew apace with the expansion of haematology and biochemistry and with the necessity for scientific control, which has constantly to be exercised over bedside problems. Bacteriological work, which in the first half of the century had found such a prominent place, began to return to the laboratory itself and eventually to become centralized in fully equipped Regional centres.

It was at this phase, in the 1920's, that it came to be recognized that the personality of the pathologist, as well as his skill, was necessary at the bedside for the proper solution of diagnostic and therapeutic difficulties. This attitude has ripened through the past twenty years in parallel with the increase in size of clinico-pathological departments, most of which are nowadays themselves subdivided. The biochemist, the haematologist, and the histologist are now always welcome in ward or theatre. The men who in this century have come to practise these arts have the mentality which delights in the precision and accuracy of a laboratory procedure and at the same time gets inspiration and benefit from the human and clinical aspects of a case; the discipline of the laboratory has been found to be a fine training for interpreting the significance of findings, whether these be laboratory or clinical. By the constant performance of tests their limitations and their snags come to be appreciated together with all the features which may invalidate a result, including some which can be observed only by personal attendance upon the patient. This is the unanswerable argument to those who think that clinical pathology demands no more than the submission of a specimen, perhaps through the post, and an impersonal examination by a competent technician.

In all large hospitals the various divisions of clinical pathology have now become separated into specialties, in the same way as clinical work. Just as there are cardiologists, gastro-enterologists, and endocrinologists, so there are biochemists, haematologists, bacteriologists, and others, each pursuing a branch of what at one time was one subject. But not so in the smaller centres, where the clinical pathologist still combines all branches of the art just as his clinical colleague still practises as a general physician. The evolution of clinical pathology in these small centres has been almost an epic. Beginning in some small room, generally in the basement or an outhouse or a hut, or any unwanted premises, and often initiated by some keen and far-sighted general practitioner, the clinico-pathological service of these small hospitals and districts has been created despite financial stringency and often lack of

encouragement, and has become in many instances the central focus of the district. The clinical pathologist has often become the key consultant of the community to general practitioner and consultant alike; an artist with the needle (and what a mess a clumsy venepuncture or lumbar puncture can be); knowledgeable about modern advances and with a laboratory which, like its larger counterpart in teaching hospitals, is usually a meeting-place for intellectual medical discussion. Here, over the inevitable cup of tea, the medical men of the district come to discuss their problems, to seek advice, and to keep themselves up to date.

A landmark in the evolution of clinical pathology in this country was the foundation of the Association of Clinical Pathologists in 1927. There are similar organizations in the United States and in other countries, whilst the formation of a European Association was completed in 1947. In England, the association was started by a group of men drawn largely from the non-teaching hospitals of the Provinces, who desired to have a society where there was emphasis on the practical aspects of pathology as applied to the bedside. The association is now one of the most flourishing in the country and publishes—in co-operation with the British Medical Association—its own journal.

The further development of the fascinating subject of clinical pathology will be an important aspect of the National Health Service. Though some of this work, especially bacteriology and histology, can be done in Regional laboratories in an impersonal manner, there will always be a far larger amount which necessitates the bringing of the patient to the pathologist or the pathologist to the patient. This, in places where distances are large and the population scattered, presents many problems. In this country, happily, the evolution of clinical pathology has not led to an attitude of mind where the patient becomes a mere number attached to a wad of routine laboratory reports among which, with a fine disregard for economic factors and intelligent selection, one result may occasionally be found which supplies a diagnostic finding. Fortunately, those who have practised the subject have been at pains to see that the personal side has prevailed, so that a clinical examination has orientated the laboratory work and the patient has remained a human problem. It is to be hoped that nationalization will not alter this typically British tradition, but there is inevitably a danger that bureaucracy may insidiously submerge humanitarianism and come to regard all clinico-pathological problems in terms of the appropriate Government form. Should this come to pass, then the fine traditions of the past half-century will disappear for ever.

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Speech as a Septic Influence.—"Professor Flügge . . . might quote the same text in support of the doctrine which he preaches that speech is a means of distributing disease germs. He has shown that from the mouth of a person who is speaking come bacteria contained in little bubbles of saliva, which after remaining suspended some time in the air are scattered through the surrounding atmosphere. . . . One may conjure up a prophetic vision of the twentieth-century surgeon with antiseptic mask, beard-bag, gloves, and sterilized robe, operating within a glass sanctuary into which no one is admitted except after the fullest disinfectant lustration." From an annotation in the *British Medical Journal* of February 17, 1900 (p. 401).

PREVENTION AND CONTROL OF INFECTION

BY

ROBERT CRUICKSHANK, M.D., F.R.C.P., D.P.H.

Professor of Bacteriology, St. Mary's Hospital Medical School

A few years ago C.-E. A. Winslow, the doyen of preventive medicine in America, wrote a book called *The Conquest of Epidemic Disease*. Although the title sounded rather pretentious and euphemistic, Winslow's object was to trace the development of epidemiological concepts about the causation of epidemic disease from the time of the biblical belief in visitations from heaven or hell, through the theories on spontaneous generation and miasms, to the present-day proof of the transmissible germ; to show, in fact, that, since the aetiology and modes of spread of most epidemic diseases were now known, the means for their control should be available.

Beginning with the acute observations of Hippocrates in his *Airs, Waters, and Places* on the epidemiology of such conditions as the ague, dysentery, and chest infections, the road to knowledge of the causation of infectious diseases has been slow and tortuous, and was blocked for a thousand years during the "Dark Ages." The pandemic of plague in the fourteenth century, which was so obviously contagious, was followed by a pandemic of syphilis about A.D. 1500 which allowed Fracastorius to elaborate his clear and convincing principles on the spread of disease by contagion, although he conceived the transmissible agent as being gaseous rather than living particulate matter. In spite of Kircher's scientific arguments in favour of the "contagium animatum" and Leeuwenhoek's microscopical demonstration of the little animalcules in the seventeenth century, the germ theory was again stayed during the eighteenth century, largely by Sydenham's advocacy of the "Epidemic Constitution," and it was not until the latter half of the nineteenth century that the genius of Pasteur and the painstaking researches of Koch firmly established the microbial aetiology of infection. By 1900 the heyday of bacteriological discovery had passed, for the causal organisms of most major pestilences—typhoid, dysentery, cholera and plague, tuberculosis, pneumonia and diphtheria, meningitis, and gonorrhoea—had been identified.

But there still remained many puzzles. The aetiological agents of typhus, syphilis, yellow fever, scarlet fever, and whooping-cough were still undetermined, while the occurrence of infection among those who had no obvious contact with the sick, and, *per contra*, the failure of others to develop infection in spite of such close contact, were still unexplained phenomena. The importance of the carrier in the spread of infection, the principles of immunology, and the factors determining the virulence of an organism are developments of the past half-century. At the beginning of the twentieth century there was still a great deal of spade-work to be done in the methods of isolation and identification of specific pathogens, so that opportunities for devising new microbiological techniques abounded. The typhoid bacillus was separated from the colon bacillus by fermentation reactions, the bovine type of tubercle bacillus was differentiated from the human type, and the botanical classification of bacteria as agents of infection became an absorbing study for the rank and file of the new race of bacteriologists who were still closely attached and subservient to the morbid anatomists. However, men of ideas like Ehrlich, Bordet, Almroth Wright, and Theobald

Smith were not wanting, and they were turning their attention to the many problems in the control of infectious disease ; searching for the reservoirs of the infecting organism : tracing its mode of spread to new susceptible hosts ; studying new methods for protecting the host against infection : or attempting to cure the infection by some specific therapy. Progress in the fight against infection during the past fifty years may best be reviewed under each of these four headings.

Progress in this field is often represented as being strikingly successful because of the rapid decline in the death rates from some of the common infectious diseases —for example, scarlet fever, measles, and whooping-cough. It is, however, doubtful if this reduction in mortality has owed much to specific measures aimed at the control and prevention of these infections, since there has been no corresponding decline in morbidity. A general improvement in social conditions, including nutrition, has probably been the main contributor to the reduction in case mortality until the new chemotherapy lent a helping hand. The case is otherwise, of course, with the intestinal infections, where there has been a great reduction in both morbidity and mortality rates.

The Reservoirs of Infection

The careful observations and deductive reasoning of John Snow and William Budd in the middle of the nineteenth century had established in pre-Pasteurian days the main facts about the spread of cholera and typhoid fever, but it frequently happened that outbreaks of these infections could not be traced to a primary case of the disease. In his studies on cholera Koch showed that convalescent cases or contacts with minor symptoms were excreting the vibrio, and these carriers could therefore explain the spread of infection by apparently healthy persons. This concept of the symptomless carrier as a link in the chain of infection was soon proved to be applicable to other infections. Koch and his associates, using the new Drigalski-Conradi culture medium, were able to demonstrate the presence of 72 missed cases or carriers of typhoid fever in a group of villages where only eight clinical cases had been reported. About the same time Park and Beebe demonstrated the occurrence of convalescent throat-carriers of the diphtheria bacillus, while later the meningococcus was found in the throats of convalescent cases and symptomless contacts, and dysentery bacilli in the stools of both contact and convalescent cases. The epidemiological importance of the carrier gradually became recognized, and in 1912 a monograph was published on "The Carrier Problem in Infectious Disease" by Ledingham and Arkwright, which, with its wealth of information, further helped to focus attention on this important reservoir of infection.

It became established that the gall-bladder was the main breeding-ground of the bacillus in the chronic typhoid carrier, and that this condition was four times more common in women than in men, particularly in the middle-aged matron who was also prone to gall-stones. In other words, a diseased organ or tissue was apparently a prerequisite of the persistent carrier condition. Similar findings emerged in the case of the diphtheria carrier, who usually was shown to have diseased tonsils or unhealthy nasal mucous membranes.

The evidence that the infecting organism persists in the tissues during convalescence in a steadily decreasing proportion of cases, which was first demonstrated for diphtheria and typhoid, has been extended to other bacterial and virus infections as techniques for the isolation of the pathogens were improved. In scarlet fever, lobar pneumonia, bacillary dysentery, Salmonella infections, and poliomyelitis the occurrence of the convalescent carrier has been well established, and no doubt these carriers play their part in the dissemination of infection. However, it seems likely that in future more attention will be given to the quantitative excretion of pathogens by the carrier and to the pathogenic potentialities of the harboured organism than to the carrier's mere existence, in assessing his importance in the spread of infection. Refinements in bacteriological techniques allow the isolation of very scanty numbers of diphtheria or dysentery or Salmonella bacilli from the throat or intestine, and such "light" carriers are often segregated in hospital until the ultimate pathogen has been eliminated, although it seems likely that they play little part in the spread of infection. On the other hand, it has been shown that the heavy nasal carrier of haemolytic streptococci is a much more dangerous source of infection than the corresponding throat carrier, apparently because he disseminates in his environment about eighty times the number of haemolytic streptococci. The convalescent intestinal carrier of poliomyelitis virus is another interesting phenomenon, for while he excretes virus in plenty he is rarely incriminated as a source of infection.

Another advance in bacteriological methods which has greatly helped in determining the source of an outbreak has been the subdivision of particular pathogens into types by antigenic analysis or by their susceptibility to specific bacteriophage. After the early work in the classification of the typhoid, Salmonella, and dysentery groups, the recognition of serological types within the genus Pneumococcus was perhaps the first step towards this subdivision of the species. Dochez and Avery in America, and independently Lister in South Africa, recognized a number of different serological types which were associated with lobar pneumonia, and this work led on to the antigenic analysis of the pneumococcus with the demonstration that serological specificity was associated with the chemical constitution of the capsular substance. As serological subdivision became extended to the pneumococci found normally in the throat as well as those associated with infection it emerged that most cases of lobar pneumonia were caused by a limited number of pneumococcal types. Thus the conception of lobar pneumonia as an infectious disease became accepted and variation in the pathogenicity of members within the species became established, although the explanation for this variation still eludes us.

The methods of antigenic analysis were extended by Bruce White and Kauffmann to the Salmonella group, by Andrewes and Inman to the dysentery bacillus, by Gordon and Murray to the meningococcus, and by Griffith and Lancefield to the haemolytic streptococci, while a biological differentiation of the diphtheria bacillus into three main types—gravis, intermedius, and mitis—was made by McLeod and his colleagues. An entirely new method of subdivision was later discovered by Craigie and Yen, who showed that a typhoid Vi phage could be adapted to lyse strains differentially, so that this serologically uniform organism is now classified into twenty-four phage types. This method of phage typing has been extended by Felix and Callow to paratyphoid B and typhi-murium strains. The staphylococcus has also been studied intensively in recent years, and has been subdivided by both serological and phage typing, an interesting phenomenon being an apparent correlation between the two methods of typing.

Besides its epidemiological value in tracing the source and mode of infection, this subdivision has also helped in the identification of some abnormal properties in particular members of a species. Thus certain types of *Str. pyogenes*, being active producers of erythrogenic toxin, are particularly associated with scarlet fever; while only two of the phage types of *Staph. aureus* produce enterotoxin. The different types of diphtheria bacillus differ in their pathogenicity for the human host, and variation in virulence and invasiveness has been demonstrated among the members of the Pneumococcus and Salmonella families.

Modes of Spread of Infection

The sanitary awakening of the nineteenth century, with its emphasis on the association between dirt and disease that led to the purification of water supplies and to the water-carriage system of sewerage, was followed by a rapid decline in the mortality and morbidity of the two main intestinal infections, typhoid and cholera. This campaign against environmental filth, led so vigorously by Chadwick and Simon, was based on the conception of atmospheric impurities or miasms emanating from the dunghills and privies that made many of our cities so disgusting; and environmental sanitation became the keynote of all programmes aimed at improving the health of the people. Dirt, dust, fomites, air, and water were claimed by Pettenkofer and his followers to be the main breeding-places of the infecting germs until, early in the twentieth century, first Flügge in Germany and later Chapin in America directed attention to man as the natural reservoir of most pathogens, which must live a parasitic existence and are unlikely to survive, let alone multiply, outside the body. The poor viability of intestinal and respiratory organisms outside the body was accepted; Flügge showed that the infective particles could be sprayed to a radius of only two to three feet from a coughing tuberculous patient, and Chapin in his *Sources and Modes of Infection* became the champion of the direct-contact spread of infection, in opposition to the view that air, water, and inanimate objects were the important vehicles. Tetanus and anthrax were admittedly derived from soil through their resistant spores, but even these organisms did not multiply there. Typhoid was much less a water-borne infection than was generally believed, and Chapin strongly opposed the view, promulgated by Power and others, that the virus of smallpox could spread considerable distances through the air. Fomites were only rarely a means of spreading infection, and in this belief he discontinued "terminal disinfection" of houses after removal of an infectious case. Chapin's views, together with Flügge's doctrine of droplet or spray infection, led to the development of the bed-isolation and barrier technique for nursing infectious patients in fever hospitals, and the success of these methods confirmed the great importance of direct-contact infection. More recently Harries has been the chief advocate of the view that the hands play a major role in hospital cross-infection.

Rifts in the lute were soon to appear. Medical superintendents found that certain diseases like measles and chickenpox could not be nursed in barrier or cubicle wards without the risk of secondary cases, while French and German workers were proving that contaminated dust could be an important vehicle for the spread of tuberculosis. It was not, however, until the years before the 1939–45 war that direct contact as the only important mode of spread of respiratory infections began to be seriously questioned again. The work of Cruickshank, Allison, and others on the part which contaminated dust may play in the spread of streptococcal infections was followed by Wells's experiments in America demonstrating that a proportion of the droplets expelled during talking, coughing, or sneezing were so small (droplet nuclei) that they could remain suspended in the air for appreciable periods of time and be carried considerable distances from the source of infection. These findings gave fresh impetus to studies on sources and modes of spread, and led to the development of methods for controlling air-borne infection by suppression of dust (oiling of floors and fabrics) and by the use of aerial disinfectants (ultra-violet light and vaporized chemical substances). The latest development in this field is the proposed use of medicated handkerchiefs to destroy the bacteria in expelled droplets before they can be disseminated in dust particles or droplet nuclei.

As for the intestinal infections, water-borne outbreaks of typhoid fever became quite rare and most cases developed in small isolated foci where there was opportunity for spread through food and fomites. Careful search, using modern bacteriological tools, usually lead to the discovery of a chronic carrier as the source, and it is obvious that if all chronic carriers could be identified the risk of outbreaks would be greatly reduced. To this end a register of typhoid carriers in this country is now being maintained and steadily expanded at the Central Enteric Reference Laboratory. It would be advantageous if carriers could be recognized before they were incriminated as the source of an outbreak; and here again bacteriological and serological investigations of all convalescent cases will help to identify the persistent carrier. Paratyphoid fever was shown by Savage to be more closely related epidemiologically to the acute Salmonella gastro-enteritis than to typhoid fever. Both diseases are most often food-borne infections, with the highest incidence in the summer months—which indicates that a much bigger dosage of the pathogen is needed to initiate infection than is the case with *Bact. typhosum*. This and other evidence that these organisms and the enterotoxic staphylococci must multiply in food before causing infection has led to improved methods in the handling and storage of food.

Bacillary dysentery, which the pioneer work of Gettings at Wakefield had shown to persist in our mental hospitals largely through chronic cases and carriers, was found in the nineteen-twenties to be occurring in a mild form in the general community, and a new member of the dysentery family, the Sonne bacillus, became recognized. Since then Sonne dysentery has established itself in this country as an endemic infection, which rose to epidemic prevalence during the late war. Although explosive food-borne and, very rarely, water-borne outbreaks have occurred, its spread is usually from case to case in a manner which is still imperfectly understood, but probably occurs in very small dosage by contamination of food and fomites. With the intestinal infections, therefore, the emphasis as regards modes of spread has been changing from unsatisfactory sanitation to poor personal hygiene: routine hand-washing after use of the w.c. and before handling food would help materially in the control of these infections.

Our knowledge about the mode of spread of virus infections has until recently been based largely on epidemiological data. Although jaundice occurred as an epidemic disease in the Gallipoli campaign of 1915, the proof that catarrhal jaundice is an infectious disease (infective hepatitis) came much later and owed a great deal to the carefully collected observations of a country practitioner, W. N. Pickles, of Wensleydale, who regarded it as a droplet-spread infection with an incubation period of

approximately four weeks, a view that has been largely corroborated from recent experience, although some observers believe there is evidence supporting an intestinal mode of spread. The American epidemiologist W. H. Frost concluded from epidemiological data that poliomyelitis was also a droplet infection, and this view is now being upheld after a period when, because the virus was found in the intestinal tract of convalescent cases, the water-borne and food-borne modes of spread were regarded as more likely.

The mode of transmission of typhus fever is a discovery of the twentieth century. Although epidemic typhus has played an important part in determining the course of history (see Zinsser's *Rats, Lice, and History*), it was not until 1909 that Nicolle and his colleagues showed it to be a louse-borne disease and not until 1916 that Rocha-Lima demonstrated the aetiological agent, *Rickettsia prowazeki*. During and after the 1914–18 war other infections—Rocky Mountain spotted fever, trench fever, and scrub-typhus—became recognized as rickettsial infections, and in recent years two others, Q fever and rickettsial pox, have been added to the list. The natural hosts and vectors (lice, rat fleas, ticks, and mites) of most of these rickettsial infections are now known, and the effective use of an insecticide in controlling the spread of epidemic typhus was well illustrated by the use of D.D.T. in the Naples outbreak at the end of the 1939–45 war.

Another pestilence about which much new knowledge has been accumulated in the past half-century is smallpox. The virus nature of the infection has been firmly established, and improved laboratory techniques—demonstration of the elementary bodies in smears, cultivation with characteristic lesions on the chick embryo, and the use of the precipitation and the complement-fixation tests—have allowed easy and early diagnosis of the atypical case. Much still remains to be discovered about the infectivity and mode of spread of smallpox, but with these new tools progress seems assured.

Hospital infection, which was such a scourge in pre-Listerian days, again became a major problem during the 1914–18 war, so that most wounded men admitted to hospital developed secondary pyogenic infection. As a result new antiseptics like the flavines and hypochlorites were introduced, but with a return to civilian practice this problem became forgotten until the late war brought it into prominence again. An intensive attack, led by the bacteriologists armed with new methods for tracing the spread of the haemolytic streptococcus and other pathogens, resulted in great improvements, such as the "no-touch" technique, in methods for dealing with wound infections. Towards the end of the war penicillin, used on a large scale prophylactically and therapeutically, achieved remarkable results in controlling both gas gangrene and the pyogenic infections.

Protection of Susceptibles

The system of dealing with infectious disease by notification, isolation, and quarantine, initiated in the last century and developed in the early decades of the present, was designed partly to afford suitable treatment for the patient and partly to reduce the risk of infection among contacts. Although sometimes a life-saving measure, as in diphtheria, hospital treatment of infections like measles and scarlet fever frequently failed to achieve its main purposes, for the patient developed secondary complications from cross-infection after admission, and often managed to infect susceptible contacts before his removal or after his return home. Although mortality rates of most infectious diseases have shown remarkable, if uneven, reduction in the past half-century, the incidence of the respiratory group of diseases has changed very little, and as many children develop measles and whooping-cough to-day as fifty years ago. Obviously some more specific means of protecting susceptibles was needed.

Although typhoid fever in the civilian population was quickly coming under control with improved sanitation, the ravages from this disease during wars was an important stimulus to the discovery of more effective preventive measures. Almroth Wright had gone to be professor of pathology at the Army Medical School at Netley in 1892, and from 1895 onwards he developed his conception of active immunization against typhoid fever by the use of killed vaccines, which was a "break-away" from the Pasteurian practice of using attenuated living cultures. He standardized the dosage and, having satisfied himself that inoculations of killed vaccine rendered the blood highly bactericidal to the typhoid bacillus, he urged the adoption of active immunization for our armies overseas. His proposal was at first rejected by the War Office, but a Royal Commission reversed this decision, and antityphoid inoculation was adopted as a standard procedure for the British Army. The benefit was not fully reaped till the 1914–18 war, when the annual incidence and death rate from typhoid per thousand strength were respectively 2.35 and 0.139, compared with figures of 105 and 14.6 in the South African War. Later, Arkwright's classical studies on the change in Salmonella bacilli during artificial culture from the smooth (virulent) to the rough (avirulent) variant led to the preparation of typhoid vaccines from smooth mouse-virulent strains, and after Felix had demonstrated the importance of a heat-labile antigen (the virulence or Vi antigen) alcohol-killed and alcohol-preserved vaccine was introduced as a further improvement.

Meanwhile, although progress had been made in the preparation and use of diphtheria antitoxin, so that case mortality was reduced to about one-third of that of the pre-antitoxin era, deaths from diphtheria remained at figures around 2,500 and 3,000, with an incidence of 50,000 to 60,000, per annum. It was known that susceptible animals could be immunized against diphtheritic infection, but early attempts to immunize man by using small doses of toxin or bacterial vaccine gave little promise of success. Theobald Smith's observations that suitable mixtures of toxin and antitoxin could be used as immunizing agents were not followed up until 1913, when Schick described a skin test for differentiating susceptible from immune persons and von Behring reported that toxin-antitoxin mixtures could safely be injected into children. W. H. Park, of New York, then became the leader in the campaign for the immunization of children against diphtheria, and his energy and enthusiasm were in large part responsible for the progress made in America at a time when, despite advances in the laboratory, Britain was still holding back. The leader in the laboratory was A. T. Glenny, who produced first diphtheria toxoid (toxin rendered innocuous but still highly antigenic by the addition of formalin), then the toxoid-antitoxin mixture (T.A.M.), then toxoid-antitoxin floccules (T.A.F.), a remarkably safe and efficient prophylactic, and lastly alum-precipitated toxoid (A.P.T.), which was shown to have greatly increased antigenic activity associated with its slow absorption and excretion. The latest development in diphtheria prophylaxis is the preparation by Holt of purified toxoid precipitated in optimum proportion with aluminium phosphate (P.T.A.P.) and constituting an antigen which is remarkably uniform, efficient, and safe in its action.

Although Britain was a late starter in large-scale immunization against diphtheria, the national campaign, begun in 1940 with A.P.T. as the antigen of choice, has in the past eight years achieved phenomenal results. Some 60–70% of school and pre-school children have been immunized, and notifications of diphtheria have fallen from an average of 60,000 in pre-war years to 3,531 in 1948, with only 156 deaths.

Wars often act as accelerators to the advance of medical science. Protection of the wounded against tetanus was first attempted on a large scale during the 1914–18 war by prophylactic injection of tetanus antitoxin at the time of wounding. Later the demonstration that both horses and men could be effectively immunized with tetanus toxoid led to the adoption of active immunization during the 1939–45 war, supplemented, in the British Forces, by passive immunization at the time of wounding. As a result the incidence of tetanus fell from rates of 15–30 per 1,000 wounded in the early stages of the 1914–18 war to less than 1 per 1,000 when tetanus antitoxin became generally used, and to rates that varied from 0.04 (B.N.A.F.) and 0.06 (B.L.A.) to 0.43 (B.E.F.) per 1,000 wounded in the different campaigns of the 1939–45 war. Knowledge about the aetiology and means of control of gas gangrene developed from studies in the 1914–18 war, when the pathology and bacteriology of this virulent infection was established, and the first controlled trial in specific prophylaxis was carried out with *Clostridium welchii* antitoxin. The value of gas-gangrene antitoxins in the prophylaxis and treatment of this composite infection is still a matter for discussion, but here again there is promise of progress in the use of toxoid for active immunization. The stimulus of war also led to rapid developments in the preparation of vaccines for protection against typhus and other rickettsial infections. Apart from living vaccines prepared in animal tissues, the only killed vaccine in use against typhus before the 1939–45 war was the Weigl vaccine derived from lice after rectal injection. The cultivation of the rickettsia in chick embryo resulted in the large-scale production of egg-yolk vaccine, which was used with remarkable success to protect the Allied troops fighting in areas where typhus was endemic.

Between the wars the field of viruses was being tilled with vigour and was beginning to yield fruit. At the National Institute for Medical Research, which had been established by the Medical Research Council to carry out organized research on biological problems, the work of Laidlaw and Dunkin on dog distemper, with the ferret as experimental animal, resulted in a practical method of immunization, and probably stimulated the fresh attack on the aetiology of influenza which led to the discovery of a specific virus by the Hampstead team. The adaptation of this virus, first isolated in the ferret, to the mouse and the chick embryo allowed its production on a sufficient scale for the preparation of vaccines, which have been used with some success in the prophylaxis of influenza. It is now known, however, that besides two main serological types of influenza virus called A and B there are antigenic variants within each of these types, so that a vaccine prepared with a particular A strain may not protect against another member of the family.

The demonstration that certain fractions of an organism —for example, the O antigen of the Salmonella group and the capsular polysaccharide of the pneumococcus—are particularly associated with pathogenicity encouraged the immuno-chemists to produce pure preparations of these fractions for use as immunizing agents. Although some success has been obtained experimentally with O fractions of Salmonella and Shiga dysentery bacilli, the most promising bacterial fraction has been the specific pneumococcus polysaccharides, which when injected in infinitesimally small amounts have proved to be protective against infection with the corresponding pneumococcus type. Progress has also been made in the combination of two or more antigens—for example, in immunization against typhoid and tetanus or against diphtheria, pertussis, and tetanus. Such combined prophylactics do not interfere with the antigenicity of each component, but seem rather to encourage better antibody production than when the antigens are used singly, and have the administrative advantage of reducing the number of injections. Combined active and passive immunization has been found to be a practicable and useful procedure against both diphtheria and tetanus.

The recent use of living vaccines represents another turn of the wheel. Lymph vaccine has, of course, long been used to protect against smallpox, but the development of a live yellow fever vaccine has proved to be perhaps the only artificial method of immunization that gives complete protection. Live vaccines of *Brucella abortus* and distemper virus have come into effective use in veterinary practice, and the B.C.G. tubercle vaccine is establishing itself in many countries as one method of reducing morbidity and mortality from tuberculosis.

Treatment of Infection

The successful production and therapeutic use of diphtheria antitoxin before the end of the nineteenth century were followed by much less successful attempts to treat other infections, from tetanus to typhoid, with specific antisera. Where disease symptoms were due to powerful exotoxins, it became apparent that these toxins were selectively fixed to tissue cells so quickly and firmly that the specific antisera could have only a prophylactic effect. This has proved to be the case with tetanus and to a large extent with diphtheria, so that it is only in cases treated in the first few days of infection that antitoxin is beneficial. Antibacterial sera had not achieved much success until anti-pneumococcal sera, concentrated by a new process by Felton, yielded such promising results as to encourage large-scale production of different type-specific antisera, first in horses and later in rabbits. However, just as this method of treating lobar pneumonia was being adopted by other countries than America, where it was first introduced, Whitby, in 1938, showed that one of the new sulphonamide drugs, sulphapyridine ("M and B 693"), was effective against pneumococcal infections, and chemotherapy quickly supplanted serotherapy. Within the next two years the sulphonamides had perhaps their greatest triumph against the largest epidemic of cerebrospinal meningitis that this country has ever experienced.

This extension of chemotherapy to infections other than the spirochaetal diseases had to wait a quarter of a century after Ehrlich's discovery of "salvarsan," and was thought at first to be another example of the specific affinity of a dye-like antiseptic for the bacterial cell. However, the researches of Fildes and Woods on bacterial metabolism indicated that the chemotherapeutic action of these new drugs depended on competitive inhibition by the sulphonamides against an essential metabolite, in this case para-amino-benzoic acid. Other analogous types of inhibition were shown to occur, and this new approach has opened the way to a rational attack on the bacterial cell. Meanwhile, in America Dubos was attempting to isolate antibiotic substances by using killed cultures of staphylococci,

pneumococci, and streptococci as the substrate for soil bacteria, and his success with tyrothricin and gramicidin was probably the stimulus which led Florey and Chain to investigate penicillin, a mould extract whose properties and potentialities as a chemotherapeutic agent had been described by Fleming ten years earlier. In the past few years many thousands of antibiotics have been isolated, but only a few have been found to be therapeutically useful. However, armed with the sulphonamides, penicillin, and streptomycin, and soon, we hope, with chloramphenicol and aureomycin, the medical practitioner can to-day tackle most bacterial infections with reasonable hopes of success. The therapeutic activity of the latter two drugs against the rickettsia and some of the larger viruses gives promise of still further successes.

Besides their clinical value in the treatment of established infection, the new drugs are by their bactericidal and bacteriostatic activity helping to eliminate the reservoirs of infection, particularly in convalescent and contact carriers. This effect was demonstrated in the use of sulphonamides for the treatment of bacillary dysentery, since the drug secured early bacteriological as well as clinical cure, and this action probably helped to curtail the spread of dysentery among our troops during the 1939–45 war. The sulphonamides have been equally effective in eliminating the meningococcus and gonococcus, and have been used prophylactically to control the spread of infection due to these and other organisms and to prevent relapses of rheumatic fever. Penicillin has also been used successfully to eliminate the haemolytic streptococcus and diphtheria bacillus from the upper respiratory tract of acute cases and carriers. A new danger, however, is the risk of the development of drug-resistant bacteria, exemplified by the sulphonamide resistant gonococcus and haemolytic streptococcus, the penicillin-resistant staphylococcus, and the streptomycin-resistant tubercle bacillus. So far, no satisfactory solution of this problem has been forthcoming.

Summing Up

With bacteriology still in its first vigour around 1900, it was natural that the parasite should be regarded as the most important factor in the occurrence of infection. The success of vaccine prophylaxis and of chemotherapy helped to establish the bacteriologist as an equal with his clinical colleagues, and for a time this new branch of medicine flourished better than perhaps it deserved. However, the development of immunology and the widening interest in bacteriology as a science in itself gradually led to the conception of infection as a struggle for existence between the parasite and its host. This oecological approach finds support in the history of infectious diseases, which after the first violent interaction, as when syphilis invaded the Old World, tend to reach an approximately balanced relationship between host and parasite, so that the survival of each is assured. For the parasite the main problem has become an easy means of transfer from one host to another. Some of the vehicles, like water and milk, have been made particularly hazardous, and intestinal infections have correspondingly declined. Blockage of the channels of spread of respiratory infections presents much more difficult problems; but dust is already being recognized as an important and controllable vehicle, and clean air in intramural spaces may some day become as commonplace as clean milk and water.

This attack on the parasite by improvements in environmental sanitation has been accompanied on the one hand by new knowledge of the reservoirs of infection and the means for their eradication, and, on the other, by successful efforts at raising the resistance of the host by specific and non-specific means. The history of diphtheria shows that no measure short of specific immunization made any progress toward its eradication, and this would seem to be the method of attack with infections like whooping-cough and measles. But history warns us again that there is no single golden rule for the control of infectious diseases, and each infection must be studied as an entity. Improvements in social conditions, and particularly in the nutrition of the community, have greatly helped in reducing mortality in most infectious diseases, but again there is no room for complacency, for the death rates from measles and whooping-cough are still many times higher among the poor than among the rich.

The following general literature is suggested for the interested reader:

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THE DEVELOPMENT OF PSYCHOLOGICAL MEDICINE

BY

JOHN RICKMAN, M.D.

President of the Institute of Psycho-analysis

The half-century which this series of essays is designed to cover also spans the history of modern psychological medicine, which is also the history of a new skill. Every advance in medical science can be related to the development of skills—in clinical observation, in the design and use of apparatus of research, in the interpretation of data obtained by the use of the apparatus, and above all in conceptualizing the problem that is being faced. To this general rule the development of psychological medicine is no exception; but since the data differ so greatly from those of the physiologist and pathologist the means by which the facts are collected also are different. Both kinds of research are concerned with answers to the fundamental question, "What goes with what?" If the data of the pathologist cannot be immediately linked with the data of the psychopathologist and psychiatrist, and vice versa, it simply means that "total medicine" has not yet found a theory which combines the two.

This article does not touch on the development of psychiatry but tries only to outline some of the changes in thought and practice that have resulted from the study of the psychological problems which patients present to doctors for solution. To summarize in a short article the changes in the last fifty years would exhaust the general reader and weary the specialist, but a description of how it all arose from simple if subtle consulting-room work (without appliances of any kind whatever) and how the range of case-taking has been extended in penetration and

in helpfulness to the patient may deserve a place in a story for doctors of doctors' work in this half-century of ferment and growth.

Doctors are not so confined as they were fifty years ago to the province of physical disease, and laymen are more ready to assume that their medical advisers are prepared to listen to any complaint, whether of body or of mind. If an examination of the body does not reveal a demonstrable disorder a doctor now hesitates before he says that a person with a multitude of complaints has nothing the matter with him. Where there is much complaining there must be something paining: if an organ does not show that there is anything amiss the person does.

Modern psychological medicine has arisen from the development of clinical skill in the doctor–patient interview, which in this specialist field is different in content, range, and effectiveness from what it was in the last century. At the beginning of this century psychiatry was under the influence of the German school of Kraepelin (1856–1926), which clung to the notion of disease entities and was absorbed in problems of description and classification of patients under certificate. Later in the 1920's another German psychiatrist, Kretschmer, working with neurotics, developed theories of the relation of disease entities with bodily types. These two schools of thought contributed ideas to psychiatry and gave the practitioner classificatory frameworks, but did not give a coherent body of theory which would integrate the enormously varied mass of phenomena in a practical way.

In America the main development of psychiatry was due to the psychobiological outlook of Adolf Meyer (1866–). His approach laid great emphasis on the interview, which was to be so conducted that the unusual features of the patient's psychology had rather to be avoided than explored, and the not inconsiderable experiential knowledge of man by the interviewer should be used to study what was known about the patient's behaviour in terms of actual overt performance open to anyone who cared to look, without making what was thought to be a fruitless search for what was going on "behind the scenes" —that is, in the unconscious. The merit of this approach is that it is available to every practitioner who takes a little trouble. The case history is examined with a thoroughness unknown to previous psychiatry. The collection of data regarding the "speechless years" (up to about age 2, obtained from parents) and the childhood years from 2 years to adolescence, and from then onwards (including, where relevant, the involutional years), is done with meticulous regard to detail and accuracy. An interpretation of the data thus collected is based on general views such as anyone of experience might form of the events and facts as found, together with a readiness to include ideas about the patient's purpose in life. It is necessary for the doctor, on his part, always to consider multiple-interrelations in the causal factors of disease and health, to make an intelligent selection of leading items when making his assessment of the case, while at the same time recognizing the need for consistency in face of the great diversity of data and of causation. (See Muncie, *Psycho-biology and Psychiatry*.) The psychobiological school, though it has improved skill in interview, has added very little to the understanding of disease processes or, for the matter of that, normal psychology, for the reason that it avoids theorizing—it lacks conceptual skill and is without challenge.

We must now turn to the vast amount of work which has been done in the last fifty years in the development of the theory, technique, and application of psychopathological research. The emphasis here given to the rise and development of psycho-analysis is certainly not due to the number of patients treated by that method (for that is comparatively small, and will probably always so remain), but because this theory has given a new dimension and therefore a new starting-point for thought. It requires no apparatus in the ordinary sense and is based on a clinical observational technique which centres on social phenomena to be found, if care is taken, most clearly in the doctor's consulting-room. Further, the psycho-analytical theory has proved so wide-ranging and integrative that (though naturally with a time lag) it is now employed creatively outside the field of clinical medicine, and is using and feeding back into academic psychology, anthropology, and education ideas which provide new starting-points for research.

A Basic Assumption

The basic assumption on which the whole of modern psychological medical research rests is simple; furthermore, it sounds plausible and one is ready to give it at least a theoretical approval. It is just this: When any two ideas come together in temporal association in the flow of one's thoughts there must be some link or links of meaning. It is one thing to toy with this notion; it is another to press it to its practical conclusion. In the psychological laboratories experiments with word associations had been carried out for many years, but the results of the research did not disturb nor did they cure anyone. Though some of those research workers had medical degrees, they had no medical responsibility for the subjects of their research, for in those days patients did not go to laboratories for help. The reasons for the sterility of this well-planned research appeared only later, and in the unlikeliest place—in the consulting-rooms of neurologists who were dealing with what was then generally regarded as most unreliable data, the outpourings of neurotics. The revolution came when the basic assumption above referred to was taken so seriously that the aetiological study and therapy of very ill people was made dependent on it, and—dependent on this —the professional reputation of the physicians undertaking this unpopular field of research and therapy turned not only on the correctness of the basic assumption but on the vigour with which the implications of it were pursued. The last is important, for, despite the reasonableness of the basic assumption, patients resist its implications—at times everyone, including the physician, tries to evade them and persuade others to do the same. Progress in psychological medicine has been made in the face of persistent opposition to the application of scientific methods of investigation to mental phenomena; indeed, strange though it may seem, it is by the study of resistance to investigation that most advance has been made. The opposition of medical colleagues to this kind of investigation and therapy, which is now not so great as formerly, was a lesser hindrance—needed less courage—than the inner resistance of the medical psychotherapist to face and overcome the objection within himself to the acceptance of unpleasant ideas. In the long run it never pays to ignore unpleasant things: they return if not dealt with.

Freud's Ideas and Discoveries

In the 1880's Joseph Breuer discovered that neurotic symptoms had a meaning. Janet made the same discovery, but did not push his observations beyond saying that the symptoms were an expression of *idées inconscientes* possessing the patient's mind; he arrived at a generalization (as had the psychiatrist Leuret before him) but did not

give particular or personal significance to the symptoms. The concept of "meaning" here implies a relation—a relation in respect to detail—to the patient's previous life. But to return to Breuer: in 1880–2 he had as a patient a girl who suffered from numerous neurotic symptoms which came on after she had nursed her father during his last illness. She had periods of dreamy confusion in which her mind was far removed from present reality and occupied with her own thoughts. It was possible to hypnotize her and get her to talk without such confusion; her mind then kept going back to ideas and impulses which she had to suppress while nursing her father, and her numerous symptoms were related to these suppressed thoughts. When the patient recalled these thoughts and "re-lived" in imagination these scenes she was for a time rid of her symptoms, but soon relapsed, so that the process had to be repeated over and over again. In the repetition the scenes dwelt on shifted farther and farther back in her life; eventually all the symptoms were removed. The cure seems to result from re-living the emotional experiences which for various seasons she had avoided feeling in the first place. The theory of the cure was that the "accumulated emotion" which maintained the symptom found an outlet, a "catharsis," in the treatment-room of the physician—that is, when it was brought to consciousness the patient got better. Freud developed this technique by abandoning hypnosis and getting the patient to talk freely, to say whatever came into his mind, holding nothing back because it might be thought to be irrelevant or distressing. The "free association rule" is the foundation on which not only psycho-analysis but modern psychotherapy rests, and it makes its demand on the psychotherapist too, for if the patient must not consider anything irrelevant neither must his physician, and the latter has the added duty of making sense of it and also of convincing the patient of its meaning.

The history of psychological medicine is bound up with the development of Freud's ideas and discoveries. These may be said to date, first, from the abandonment of the use of hypnosis as a means of extending the range of exploration of the patient's mind; secondly, from the persistent study of "resistances"; and, thirdly, from the analysis of the phenomena arising between physician and patient.

In the course of the kind of treatment we are now considering two things are invariably met with: the first is "resistance." The patient's mind seems incapable of taking an objective view of the procedure, "forgets" the free association rule or pleads that certain ideas should be made exceptions to it, and becomes preoccupied with what the analyst must be thinking about the thoughts disclosed or about to be disclosed. In the hypnotic treatment the patient was urged to remember, and the amount of effort expended in recalling painful ideas and experience gave a measure of the "resistance" to their recall. In the free association treatment there is no urging, but attention is directed to the reason for the tardiness of the mind to master its own content. It becomes apparent (to both parties eventually) that something is happening in this social relationship of two people, physician and patient: the patient cannot recollect directly—the resistances are too strong—but he is "transferring" on to the analytical situation some of the undischarged emotion which he could not deal with in the critical phases of his development. This is the second of the things invariably met with. The therapeutic co-operation between two adults has superimposed on it all kinds of emotional cross-currents from the past of which the patient was consciously quite unaware, or to a strength that he could not believe possible. This past situation, transferred to the present and dominating the physician-patient co-operation, is "the transference situation." The treatment consists in disclosing to the patient the operation of these early and buried impulses and seeing them in their past and present setting; the art of the treatment lies in the maintenance of a quiet, interested, objective personal relationship throughout the storms and confusion of these transference phenomena; "the science of the treatment," so to speak, lies in the employment of the simplest possible technical (theoretical) aids to the understanding of what is going on.

We may at this point consider an essential feature of this kind of research and therapy—namely, the capacity to listen: to listen without preconceptions and without impatience. This is a difficult accomplishment and takes years of practice. The physician needs to be utterly passive to impressions and to be not unduly hastened to action by a therapeutic urge (diagnosis and exploration must come before therapy), nor must theories intrude and bias contemplation of the facts.

The data provided by following the free association rule (and the transference phenomena) are given some sort of order if the basic assumption is really made basic to the work. (The patient's "resistance" frequently challenges this assumption; it is usually, if not invariably, a counter-attack to cover a sore spot.) Out of the experience of this rule and this simple notion Freud was enabled to construct a theory which gave meaning to neurotic symptoms, to hallucinations, and even to dreams.

Freud's Theory of Dreams

Without the basic assumption dreams would have remained an unsolved riddle, and without a solution of the dream problem neuroses would have been left without their key. In the first place it is necessary to distinguish between the manifest content of the dream and another, latent or hidden, content. The former is what the dreamer remembers of his dream—it is in consciousness; of the latter we will first assume that it has sense if we can but find it. Employing the "basic assumption" and free associations to elements of the remembered or manifest dream, it becomes clear that the dream elements represented a focal point in a number of trains of thought—that is, the dreamer makes a condensation of a number of thoughts all of which are represented in a single dream element. Another feature of the dream-work is the tendency to shift the accent from an important theme on to a trivial one—that is, there is a displacement of the emotion. A further peculiar feature is that a thing may be represented by its opposite; that is to say, it seems as if there is a part of the mind which can tolerate contradictions; and, finally, there seems at times to be a process at work to make the jumble look sensible and coherent. The importance of this study of dreams lay in the fact that by these simple devices of interpretation—that is, of undoing the disguises employed in the dream-work—light was thrown on the processes going on in the unconscious mind, or, more strictly, we are helped to make inferences about the interplay between different parts of the mind. The manifest dream is that part of the total dream process which is accessible directly to the conscious mind, but, by employing the basic assumption to free associations to the dream elements and the devices of interpretation above mentioned, thoughts are disclosed (and their relation to the manifest content is recognized by the dreamer) which seem to belong to another part of the mind and personality—to the unconscious. Something like a force seems to be keeping the

two apart; the urging to remember painful episodes in the hypnotic treatment and the "resistance" to freely associating justify the use of some such concept. Freud's most simple rules for the unravelling of the meaning of dreams may be described as the main tool of research and therapy in this field. They have often been challenged; some think they have added materially to them, but no one has found in them anything superfluous. Freud's theory of dreams provides the main conceptual structure on which psychodynamical research is built, and therefore on which therapy is based.

The Problem of Treatment

When the urgings of the hypnotist were abandoned in favour of a passive observation by the therapist of just whatever the patient liked to say or to impute to him (or to try to manipulate the relationship between them) the focus of attention of the therapist is turned to the forces in the patient's mind as the immediately significant data, and these data in strangely large proportion are apparently irrelevant to the immediate situation. The therapist is pictured by the patient to be playing all manner of roles; and it soon becomes apparent that these roles have relevance to periods and episodes of frustration in the patient's past life and even to early childhood.

When sufficient care is given to detail, and the phenomena to be observed are not blurred by the impatient interferences of the therapist—how difficult that task is, as beginners only later discover!—a new sort of mental functioning becomes apparent: it is primitive, infantile, and unconscious. One of its important features is the part which bodily impulses of the most elementary kind play in the personal relationship which the patient's fantasy elaborates. It is not a simple "falling in love" but a complicated mixture of love and hate, tenderness and aggression—put simply, both attraction and repulsion, "ambivalently" mixed; it is a mode of a relationship which is strange to adult ways of thought. It seems that the free associations in the transference situation disclose two new things: first the way in which bodily-centred impulses of instinctual origin (in the mental sphere the part of us which is nearest to the animals) find representation in our imagination and outlet in our action, and also how they become transformed into the bonds which tie us in love and in hate to those nearest and dearest to us, and also by displacement to our kind generally—this throws light on our cultural life and may provide a clue to that great gap which separates us from the animals. We are not only more intelligent than the beasts, but we have a more flexible emotional life; if we are frustrated in our love (and who is not?) we displace our longing to another and seek satisfaction from a new source. Animals pine for a lost companion; man uses his frustrations, for the most part, to build, under the pressure of painful loss, an inner world—a private zone of culture—where he can work through his privation, however long and devious the path, to a solution of his longing. The richness of that inner world, which animals seem to lack, is the result of overcoming mental pain; we seem to differ from the animals, too, in being able to share with others the benefits we gain from our private zone of culture.

The second thing that may be observed is that, though there are in fact only two people in the therapeutic situation, the patient frequently behaves as if there were three or more—that is to say, he takes the analyst as the object of his impulses and also feels a constraint as if another person's rights and feelings had to be taken into account at the same time. It seems as if from an early age of personal or mental development the individual cannot help dealing with two people at a time; if the third party is not actually present the mind unconsciously imagines him or her to be there. The character of the behaviour, and indeed the mood, of the individual and his confidence or diffidence in life generally, as well as his capacity to co-operate with his fellows, are greatly influenced by his relation to this third party. (The obscurity of these last statements may be perhaps diminished in a later consideration of this important topic.) With a perhaps aphoristic inexactitude we may say that the barrier between human psychology and sociology is broken down when account is taken of the unconscious influence of "the third party" in the relation between two people. (As this touches on society, it may be one of the most momentous discoveries in social history.)

By taking a few liberties with dates it is possible to arrange the dominant ideas into four periods.

First Period (1896–1914): Development of a Libido Theory

As has been said, one of the things disclosed by the free associations is the strange unadult nature of the impulses which the unconscious harbours. They are primitive and erotic and the conscious mind repudiates them; indeed, much of the above-mentioned "resistance" is a manifestation of this repudiation. Man appears to be unique in having two types of sexuality: an infantile kind, which persists in the unconscious, and an adult kind, which "crystallizes" at puberty. It is the persisting influence of the infantile type which leads to abnormalities of a sexual nature in the adult and largely accounts for unhappiness in married life, and it is also one of the elements in the causation of social maladjustments, including neuroses.

The sexuality of the infant—the erotic desire for another person or part of that person—is in the early days characterized by a mouth-to-nipple relationship. The infant is predominantly a "mouth animal": what it does with its mouth is exciting to it and has greater emotional value than have other activities. In fantasy the mouth activities give it control over the object of its desire and thus minister to its sense of power; they also give that feeling of access of pleasure, even ecstasy, which is characteristically erotic. Later in infantile development defaecation and urination (unlike the early oral and later genital activities) do not necessarily involve physical contact with another person, but in the infant's fantasy they provide a means of doing something to people. A personal and bodily substance is held in control at an orifice and then is expelled, not into the void—the child's mind peoples every cranny of its world—but towards those on whom its thoughts rest. A bodily substance and bodily action which biologically have nothing to do with sexuality are used by the imagination as the medium of erotic play and personal relationships. In the course of development the genitals take the primacy. These organs above all others have the power to discharge the sexual tensions of the body and at the same time to bring the individual psychically into a specially close relation with another person. The increasing urge to sexual mastery and possession of the desired object, in imagination as well as in the act, brings with it a new, or rather an enhanced, source of danger—that of rivalry with another person of the same sex, typically a parent figure in the unconscious. There is rivalry in the earlier ("pre-genital") activities also, but the unification of erotic activity and the clarification of sexual objects and aims, which reach a climax with the primacy of the genital organ, increase its

influence in personal relationships. The Oedipus complex —that is, sexual attraction to the parent of the opposite sex and hostility to the one of the same sex—is the earliest social relationship which the individual experiences. This difficult period of development is reached and usually in good part solved by the age of 5. These stresses are veiled from adult recollection by an involuntary and active forgetting, but they reappear when the effort of urging under hypnosis overcomes the resistance, and, as has been said, spontaneously and with less distortion in the transference to the therapist.

Extension of the Theory

In the course of his work Freud found that his neurotic patients remarkably often presented scenes of seduction in infancy, in a detailed and precise way, and these scenes fitted into the picture of the symptoms; but on trying to get objective verification Freud found no substantiating evidence. This was at first felt to be a blow to his previous findings—that a disturbance of the development of the sexual impulse due to active interference was one of the main factors in causing neurotic illness. Then he took a courageous and momentous step in his theoretical constructions: these events had not occurred objectively but subjectively—that is, they were occurrences in the unconscious, they were fantasies which were important to the child at the time. These fantasies were repressed but retained their urgency, not to say clamorousness, in adult life—not, of course, that the adult is aware of the cause, but he is aware of the effect, the inner unrest. A new dimension was thus given to scientific thought by this extension of theory—what happens in the world of imagination obeys the laws of that world and can influence behaviour and a person's outlook on life; medicine and science need no longer be confined to the physical realm but had a new field to explore and conquer.

An indispensable addition to the theory was introduced with the notion of "cathexis"—the concentration or accumulation of "mental energy," the nature of which is obscure, in some particular channel. When an object is "cathected" that object has a particularly strong interest for the person. This energy may be displaced from one object to another—for example, from a father figure to a representation of the father in later life: first on to those who stand *in loco parentis*, such as schoolmasters, and later to office chiefs, rulers, and so forth. Combining this concept with that of the unconscious, it is clear that the object in which the mental energy is invested need not be in the focus of conscious attention, nor need the person be aware of how much he is tied in bonds of interest (love and/or hate) to the object. Further, there is a linking of the cathexes in the unconscious, so that the characteristics of the early cathexes tend to persist in respect to later ones in the same series—that is, the patterns of behaviour which characterize early object relationships tend to be repeated in later object relationships of the same type.

Second Period (1914–23): Aspects of Ego Development

The ego itself, it was thought, could be the focus of this interest or cathexis, and the love-impulse, or at least a part of it, might take the self as its object—as happened in the myth of Narcissus. But "narcissism" is not only a peculiar and somewhat perverted manifestation of the love life; it seems apt as a descriptive term of a phase that the young usually pass through, when attention is focused on the body's strength or its graces. Closer observation showed that it describes also an attitude towards those who are derived from the self, such as one's children, or objects with which there is a close, but maybe quite unconscious, identification: a self-love flows over to them and they are enjoyed less for what they actually are than for being an embodiment in the external world of what the self once was or would like to be. From this last point it was but a step (but not all steps are easy to take) to see in the attitude to an idealized object of the ego some of the primitive, but by displacement loftily aspiring, relation to the self. An "ego-ideal" thus absorbs some of the available object-cathexes, so that those whose ego-ideals are overstrong display a restricted capacity for an adaptable and kinder object-love—"reformers" trying to shape the world to their own (often rather over-simple, if not infantile) ideas seem to exemplify this tendency.

The notion of cathexis leads to the view that the distribution of mental energy in the field of psychic life may be considered quantitatively; in the instance given the quantity of "devotion" or love is portioned out between the persons ostensibly served and the image upon which they are being moulded. To the reformer himself his conduct seems to be one of selfless devotion to others, while to the rest of the world he may seem rigid in manner, self-centred, and ungenerous. Both views are in their way correct—the frames of reference are different: the first takes its reckoning from the energy put into the ego-ideal, the second from the meagre amount of personal love (object-love) displayed. This notion of the distribution of the quantities of mental energy is not to be restricted to that which is, so to say, visible in overt behaviour: the artist and scientist, the mystic and the lunatic—for that matter all of us—have inner worlds of fantasy in which are deployed and expended considerable quantities of mental energy. Whether that inner labour results in anything which is socially applauded or has social uses varies with each individual. But, useful or not socially, it is a source of gratification to the individual; it gives, if it is in low degree, that meed of pleasure without which mental life of human standard seems not to operate; when in high degree, it gives that rare sweeping "oceanic" exultation of spirit and creative ecstasy which the artists, of all men, can best communicate to their fellows, and which it is our humble duty here merely to explain.

Third Period (1923–32): The Ego and the Id

How do we animals come to have an ego-ideal? Of what experience is it a product? Is it universal and invariable or confined to idealists? Do "really normal" people possess one, or are the "really abnormal" alone of mortals without one?

Reverting to the early work again, the patient's unconscious mind was found to contain active elements which resulted from incompletely solved emotional experiences: these, to be sure, were foci of illness, but the same principle is seen—depending on the circumstances—to be operative in a constructive or "ego-cohesive" direction as well as in a neurotic (and particularly in the psychotic) "ego-destructive" tendency. In the early stages of our development, perhaps because of an underlying bisexuality, the individual is oriented to two people at once, typically the two parents; the amount of positive or friendly cathexis which is attached to the parent of the same sex becomes incorporated in and attached to the ego, which henceforth acts as an internal representative of a once external object—a parent—guiding and supporting the ego in its struggle with its own unruly impulses. Born of a longing for the parent's approval and affection, the ego seems to split into two functions—an executive part (the

ego proper), and a critical, parent-derived part (the super-ego), which watches the ego's behaviour respecting the crude impersonal instinct-driven part of the personality called the "id."

When referring to the treatment situation it was said that the patient attributes to (or "projects" into) his doctor all kinds of roles, and at times behaves as if a third party were present from whom the communications about to be made must be kept secret. We are in a better position now to "place" these phenomena—they are manifestations of those parts of the unconscious mind with which the ego is dealing—namely, with the id and the super-ego. The task of therapy is to bring about a reorganization of these three elements of the mind so that they work together in harmony; it comes about when they are confronted with one another in the present—that is, when the patient comes to recognize that, though his id is primitive and amoral, it is a tolerable part of the total personality. At the same time there occurs an amelioration of the severity of the super-ego which, though, broadly speaking, it is patterned on a parent figure, is in fact in its early stages based not on what the parent actually was but what he was fantasied to be—another instance of the influence of fantasy.

(A study of the ego-ideal, or super-ego, is of importance for understanding some of the phenomena of hypnotism and even of autosuggestion: the hypnotist is endowed with the qualities of an ego-ideal and there is a consequent compliancy towards him. The more disguised form of suggestion, such as with placebos, probably follows this pattern—that is, on to the person of the doctor there is projected infantile fantasies concerning his magical qualities. In the long run this sort of patient-doctor relationship proves a hindrance to the acceptance of a more rational medical co-operation between physician and patient.)

Fourth Period (1932 to the Present): Aspects of the Development of Object Relationship

The severity, the sometimes fantastic severity, of the super-ego led to a closer study of the aggressive component in the personality. Going back to the early days of personality development, it seems that the infant has to effect a working arrangement between two opposed tendencies —of love and hate—and furthermore that his love and hate are directed to the same objects—once again the parents. When our feelings towards any object are such that we wish more of it, want it closer to us, and hope that its like will never perish from the earth, we may be said to love that object, and to us it is a "good object." When our feelings are the reverse, when we want less of it, want it farther away, hope it and its like will cease to exist, we may be said to hate that object; to us it is a "bad object." For love and hate, good and bad, we may, on this viewing, substitute the simpler concepts of motion towards or away from, more or less, construction or destruction. These two opposed tendencies are at work in the infant's relation to its first love object—the mother's breast. On this it lives; hate for it brings inevitably the pangs of hunger: emotional conflict is from the beginning a desperately important thing. Frustration magnifies the hate—that is, makes the object still more bad—and yet the need for the breast makes the infant desire it as a thing which stills physical discomfort, so it is at times thought of as a "good thing." At this stage the child is a "mouth animal"—that is, the instrument by which it attains dominion over its object is that which incorporates the object within itself: mastery of an object entails internalizing it. The self thus becomes filled with "good" and "bad" objects—"good" if the mood at the moment of internalization is friendly; "bad" if it is hostile. There are therefore dire and, indeed, lasting consequences from the use of the expedient of "projecting" its own emotional state upon the object. "Good" and "bad" have at first no moral connotation; that may come later, but can be expressed in terms of movement nearer, a desire for more, etc., or the opposite: we are dealing here with the pre-moral stage and pre-social stage of development. When the self is filled with "bad internal objects" its greed for more and more "good" ones increases, to neutralize the bad; hence a vicious circle is developed, because greed begets guilt. As development proceeds these internalizations take on more and more the character of the actual objects, so that, to jump several stages, the person feels that he embodies the attributes of his parents. In passing we may note that savages, still in this animistic stage of object relationship, imagine that if they eat a lion's heart they will be imbued with courage; the idea is found also in some religious rituals.

Speaking descriptively, the ego is a boundary phenomenon between an internal world (an "internal society," it might be called, since the unconscious seems to be almost exclusively preoccupied with personal relationships) and an external world revealed through the sense organs. Behaviour can be viewed as the result of the ego being driven by (id) instinct-impulses but curbed by that representation within itself of parental authority (the super-ego), while at the same time the ego has to adapt itself to and master portions of the external world. But behaviour may also be regarded (and without contradiction) in a rather different way—namely, as a container of cathected objects which may work in a unified way or which may show oscillating, unstable, divergent tendencies according as the grouping of forces within the ego is cohesive and unified or disruptive and diversified. These internalized objects (or super-egos) may be pictured as having an arrangement in depth; the most primitive are the most deeply buried, but with each "layer" (representing a phase of development) influencing the deposition of, and the freedom of, movement in the more superficial layer above it; and, furthermore, and more difficult to conceive, in each "layer" the same objects (the parents, siblings, and other relations, or their surrogates, are always the central figures) recur again and again. So we find, for example, parent-regarding tendencies of differing degree of primitiveness (or, on the other hand, of complexity) interacting with each other, the resultant influencing behaviour. The "cathected internal objects" should be distinguished from mere memory traces. The unconscious is not a sort of card-index drawer of photographic images; a better analogy would be a group of objects (people or bodily parts of people) being constantly rearranged and manipulated in moods of love and hate, but unconsciously, by the individual concerned, while at the same time he is similarly manipulating objects in the external world, in the "external society." There is a constant interplay between these two manipulations, achievements, no matter how sublime or base, are made not alone for their effect on contemporary society or posterity, but also to adjust the relationships in the "internal society," that intrapsychic constellation of social and personal forces which is an ever-present and inalienable heritage of our past experience and development.

Now to return to the early stages of this eventually elaborate object relationship: there is stability in our emotional orientation to, and hold upon, objects when we are able to recognize at the same time their "good"

and "bad" qualities, when, despite anger-rousing frustration, we can keep our orientation to them and our good regard unchanged. One of the several ways by which this mature attitude is achieved is by turning against the self part of the aggressiveness which the frustrating object rouses in us; we then become severer with ourselves for our aggressive impulses towards objects that we hold to be good, and the object is spared at the cost of the self; we suffer pangs of guilt. Pain thus caused is, as it were, cherished by the self (or at least there is "resistance" to its disclosure and removal) because it is part of a device for protecting a good object. Another way by which the mind is eased of its load of guilt is by "restitutive acts"—that is, making good the damage done in moods and moments of anger. Sometimes "restitution" thus based is the main motive of an adult's life; the indefatigably, almost wearisomely benevolent people commonly react lifelong to impulses of great strength which once operated at a nodal point in their emotional development, and as the whole process is unconscious it pursues its course usually unchanged by time and circumstance. Apart from more extreme cases, the restitutive reaction to unconscious guilt plays a large part in the drive towards creativeness which differentiates us from the animals, whose work usually perishes or becomes indifferent after the act of eating, of copulation, gestation, and lactation. Man combines with his fellows in his restitutive work, as he sometimes combines with others in his destructiveness. From this recognition of the need in ourselves and in others to restore and create, from the unconscious feeling and sharing of the guilt of destructive impulse, rises a community of feeling for the restitutive and constructive urges: in these feelings we find some of the roots of religion, art, and science.

Other Workers in the Field of Psychotherapy

Two names are, or used to be, commonly coupled with Freud's—Jung and Adler. The latter employed the genetic method of approach—that is, he tried to find out how the patient's present condition and symptoms can be explained by reference to his past experience; but he narrowed the range of his theory unduly by an over-emphasis on the will to power. His ego psychology was too simple to be professionally useful, though it helped many others to write popular rather than scientifically penetrating articles. Jung's work is different. In so far as I understand his complicated and seemingly mystical theories, Jung holds that in addition to the influence of past personal experiences there is also and always the influence of the collective unconscious shaping the destiny of the individual. This may of course be true, but from the point of view of science (and therefore its application in medicine) such general theories are of less importance than a step-by-step process of explanation of the influence of events that can be traced in a sufficiently thorough investigation. In the thirty-five years in which Jung's views have been developed in detachment from the history outlined above they have never attained such strength of articulation as to embody a quarterly journal or any cohesive library series of books; the absence of such collective and conscious utterance puts the views of this school at a disadvantage.

Returning to the main line of psychopathological development, which for vigour and imagination is almost exclusively psycho-analytical, mention may be made of four workers beside Freud (1856–1939). Sandor Ferenczi (1873–1933) was also a clinician of the highest imaginative capacity who grasped the full implications of the transference situation and thus widened the range of therapy; his study of the part played by the homosexual impulse in the aetiology of paranoia and the developmental stages of the sense of reality were useful in the study of the psychopathology of the psychoses. Karl Abraham's (1877–1925) work on manic-depressive disease did a similar service to the psychodynamic study of that disorder. Melanie Klein, using the extended application of transference analysis employed by Ferenczi to the study of small children, developed theories of object-relationships and depressive and schizoid conditions which have proved of great value in the study of neuroses and psychoses. That the last-named person is not a doctor or an educationist or a psychologist by training and yet has added to the specialist literature in a region of considerable clinical difficulty emphasizes the fact mentioned earlier that in research work the acquisition and employment of special skill are of paramount importance: old skills alone do not break new ground. Ernest Jones more than any other worker than Freud has applied psychodynamic ideas to a multitude of fields.

Value of a Common Frame of Reference

At the close of the last century there was a lack of a medium of communication between doctors in respect to the aetiology, symptomatology, and therapy of the psychoneuroses, and the same was almost true of the psychoses. One man's guess was as good as another's, since none of them produced a theory wide enough or elastic enough to act as an integrator of thought: a general psychopathology was lacking. The value to medicine of the ideas outlined above lies chiefly in the fact that they provide a frame of reference, a means of communication between practitioners and students. One person may put more emphasis on one aspect, another on another, but at least everyone who studies the subject at all will know where his views fit in, and where they do not, in a widely ranging theoretical structure.

The practical professional consequences of this general theoretical structure are of considerable importance. First, there can now be a greater mobility of professional personnel—for example, from in-patient mental hospital with psychotics to out-patient work with neurotics; the child-guidance and delinquency clinics need not be separated from the hospital work by lack of common ideas. Secondly, the young practitioner who takes up psychiatry has got a lively body of ideas to bite on, to struggle with, master, and improve—it would be no longer said to a beginner proposing to go into a mental hospital, as was asked of me, "Is it beer or whisky which brings you so low?"; nor do young psychiatrists when considering a change of job ask first of their young colleagues what are the sporting facilities of the other hospital, but what are the opportunities for study or research in psychodynamics. Flexible theories vigorously applied improve morale.

Applications and Effects of the New Ideas

The provision of a technique for the study of the development of the human personality, carried on with vigour, courage, and discrimination over a period of fifty years, leads almost inevitably to the practical application of the findings in as many fields as the theory covers and there are research workers ready to use the new material. Perhaps the reason why practitioners of psychological medicine are asked so often to contribute to technical discussions held by professional men in other disciplines than medicine is because a clinical study of psychodynamics

inevitably leads to investigations of the interaction of the individual with the institutions of society and to an attempt to discover the motives which lead to the individual's interest in science or art and his need for religion, politics, and sport.

The work began with the need to cure adult hysterics and obsessional neurotics, but it soon became clear that there were infantile neuroses which reappeared in early adult years (the first psychodynamic treatment of a child, by a sort of child-guidance technique, was undertaken by Freud in 1909); the application to psychotics in and out of institutions came later.

The barriers which separated medicine proper from insanity and the neurotic from the normal have begun to break down. Clinical medicine, which has never been blind, has acquired a new interest and grasp in listening not merely to the sound of organs but to the voice of the whole personality seen in a social setting. If the contribution of psychological medicine to general medicine could be summed up in a single sentence, one would say that it has given a new dimension to the medical interview. The study of psychodynamics has progressed step by step with the improvement of clinical skill applied to discourse between doctor and patient: as in science generally, so in psychological medicine, progress consists in an ever-developing scrutiny (in this case without the aid of apparatus) of what lies in the field of observation. Nowadays we can get more out of a consultation than could be got before—that is to say, clinical skill has been increased.

Conclusion

It was said that the psychodynamic ideas outlined above have given a new dimension to medical thought; in no branch of medicine is this more true than in psychiatry. That the child is father to the man and that the child models himself on his parents have long been guessed, but how the process worked was not realized. These studies have led to a way of looking at the growth of personality in health and disease which is valuable because it provokes further thought (one of the best criteria for assessing the worth of a theory); psychiatrists, while developing other techniques for the empirical treatment of mental disease, find themselves, wittingly or not, when trying to explain the behaviour of their patients, employing some or most of the ideas here so briefly sketched.

On this occasion it may not be out of place to recall that the key idea to this great advance in medical theory and technique was published just fifty years ago: Freud's *Interpretation of Dreams.* A clinician, without laboratory aids or other such devices, by the closest attention to the material before him, unpromising and the least worthy of scientific care as it was then thought, changed his specialty out of recognition and raised the potential of every doctor's clinical interviews.

"In the first instance, when the illness first came upon me, I seemed to be aware of what was about to happen. I became powerfully impressed with the idea that the Devil was about to seize me, and I felt convinced that the only way to meet him—if efficient way there was—was to remain awake waiting for him all through the night, and combat him in a naked condition. I therefore threw off all my clothing, although it was a bitterly cold February night, and there awaited the Evil One." "The Late Mr. John Ruskin: Mr. Ruskin's Illness Described by Himself." From the *British Medical Journal,* January 27, 1900, p. 225.

FIFTY YEARS OF TROPICAL MEDICINE

BY

J. S. K. BOYD, O.B.E., M.D., D.P.H.

Director, Wellcome Laboratories of Tropical Medicine

The progress which has been made during the past fifty years in the field of tropical medicine is so vast that no adequate account of it can be given within the compass of a short article. Inevitably many matters which are far from unimportant must either be omitted or be given but scant reference.

The discovery of the relationship between malaria and mosquitoes, made at the end of the nineteenth century, gave both impetus and direction to research along similar lines in other tropical diseases. Several hitherto unrecognized pathogenic parasites have been identified, and in many cases the part played by an intermediate host in transmitting the disease to man has been demonstrated, thus allowing new and precise methods of prevention to be applied. In these investigations much fresh ground had to be broken. At first little or nothing was known of medical entomology or parasitology, while microbiology, though a rapidly expanding science, was still in its infancy. Most of the detailed knowledge of these subjects that is now available has been amassed in recent years, during which time both laboratory and field specialization in the different branches may be said to have evolved. Important work has been done by specially appointed bodies such as the Plague Investigation Committee which worked in India under C. J. Martin, the Commission under Sir David Bruce appointed by the Royal Society to investigate sleeping sickness, the Kala-Azar Commission working under the Indian Research Fund Association, the American Yellow Fever Commission, and various teams sponsored by the Indian Research Fund Association, the Rockefeller Foundation, and the Medical Research Council.

In matters of therapy no important new "herbal" remedies have been discovered, although some advances have been made in the extraction and purification of the active principles of those already in use. Investigation along the lines of immunology yielded some valuable vaccines for prophylaxis and antisera for therapy, but the latter have become less important with the advent of specific chemotherapy and of antibiotics.

Vitamins were first identified during this period, and the aetiology of deficiency diseases, such as beriberi and pellagra, was explained.

Some credit for the progress made must be attributed to the stimulus of the two world wars, during which the presence of large numbers of troops in unhealthy tropical surroundings was an incentive to intensive research—some, as for example the work on malaria with human volunteers, of a kind which could not have been carried out in less urgent circumstances. Financial restrictions, the stumbling-block of most research workers, ceased to be of significance, and efforts on an unprecedented scale were made to solve outstanding problems. The results achieved were in some cases of the greatest value, and must be classed among the best of the few good things which emerged from these wars.

The practice of tropical medicine calls for an intimate knowledge of subjects which play only a minor part in the normal medical curriculum. To meet this need special teaching establishments have been founded, of which we have in Britain the London School of Hygiene and Tropical

Medicine (with which is affiliated the Ross Institute of Tropical Hygiene) and the Liverpool School of Tropical Medicine. In India, the Calcutta School of Tropical Medicine was for many years under the direction of the Indian Medical Service, while more recently, in Australia, a School of Tropical Medicine was established by the University of Sydney. These Institutes are engaged not only in teaching but also in research, both at home and in the Tropics, and have made valuable contributions in every branch of their special subject.

Malaria

Malaria is the most important of tropical diseases, and in consequence has been widely studied in all its different aspects.

Life-cycle of the Parasite

It was long believed that the sporozoite injected by the mosquito into man entered a red cell and multipled by schizogony until parasites were numerous enough to produce symptoms. A suspicion that this process might be of a more complicated nature was aroused by the observation that benign tertian (*Plasmodium vivax*) infection, when induced by blood inoculation, was cured by quinine, whereas mosquito-bite infections usually relapsed after similar treatment. This suspicion was deepened by the discovery of exoerythrocytic or tissue forms in chicks infected with *P. gallinaceum* and by certain observations made in experimental human infections by Fairley and his colleagues in Australia. Nevertheless, exhaustive examination of tissues obtained by ordinary methods gave uniformly negative results, and it was not until hyper-infection was induced, first in monkeys with *P. cynomolgi* and later in human volunteers with *P. vivax* and *P. falciparum*, by Shortt, Garnham, Fairley, Covell, and Shute, that dividing forms were found in the epithelial cells of the liver, thus demonstrating conclusively the exoerythrocytic development of the sporozoite. This discovery is not merely of academic interest but is closely linked to still unsolved problems of causal prophylaxis and prevention of relapse.

Mosquito Destruction

Early attempts to eradicate malaria by destruction of larvae were, with a few notable exceptions, disappointing. The methods then employed—canalization of streams and the oiling of stagnant water—were relatively inefficient and involved much recurring work which, in sparsely populated localities, was too costly to be practicable. This was well shown in the 1916–18 campaign in Macedonia, when all attempts at destruction of larvae failed to yield a significant reduction of mosquitoes.

At a later date, when more became known about the malaria-carrying properties of different anophelines, better results were obtained by "species control." By studying and taking advantage of the individual, and often peculiar, habits of the carrier species it has on occasion proved possible to devise some simple yet highly effective method for the control of this particular species, which can be applied without having recourse to the expensive "blunderbuss" technique needed for the destruction of all the different mosquitoes in the area. Such special methods are now used successfully in various parts of the world, good examples being the control of *Anopheles melas* and *A. gambiae* in Lagos and of *A. leucosphyrus* in North Borneo.

The most important advances, however, have been made in the materials used for destruction of larvae. The original method—oiling—though effective when thoroughly carried out, was laborious and ill suited to certain types of water. At a later date dusting with paris green was introduced, and in some cases proved better. Both these larvicides have now been superseded by D.D.T. dissolved in oil, which is more economical (one gallon will treat the same area of water as ten to twenty gallons of plain oil), much more efficient, and more persistent in action. This preparation can be applied either by hand-sprayer or, in inaccessible regions and on a larger scale, by aircraft. Such wholesale application has the disadvantage of killing many other insects besides mosquitoes, and needs careful control.

Until recent years the destruction of adult mosquitoes played a minor part in the prevention of malaria, although, with the advent in the middle 'twenties of atomized sprays containing pyrethrum, the comfort of the resident in the Tropics was greatly increased. During the first part of the second world war pyrethrum-spraying as an anti-malarial measure was used on a large scale in Southern India, and a significant reduction in incidence was claimed. D.D.T. is now employed for this purpose, and has the advantage of being non-volatile, so that when applied in suitable form to the walls and roofs of dwellings it persists as a fine crysalline deposit for a period of months, and poisons any mosquitoes which become contaminated with it. Even this method has its limitations, for, while it kills mosquitoes which alight inside the hut before or after feeding, it is quite harmless to other species which habitually fly in and out without settling except when biting. Into this latter category come certain well-known malaria carriers, a fact which emphasizes the importance of having an exact knowledge of the habits of each species. In some cases "gammexane," another potent new insecticide, has succeeded as a "residual" insecticide where D.D.T. has failed.

By attacking both larvae and adults with these modern weapons it has in certain places been possible to exterminate the entire mosquito population and hence remove all risk of malaria. Islands such as Cyprus, where a campaign along these lines has just been completed, are ideal for all-in measures of this kind, as reinfestation can be prevented by quarantine measures; but even in less fortunately situated localities it has proved possible to effect and maintain a reduction in mosquitoes sufficient to influence malaria incidence.

Treatment

"Many drugs have been employed in the treatment of malarial disease, and many drugs have some influence on it; all sink into insignificance in comparison with quinine. In serious cases, to use any drug to the exclusion of quinine is culpable trifling." Thus wrote Manson in 1900, and for many years these words were unchallenged. In some ways they are still true, for quinine holds its place as a schizonticide, and in the opinion of many is the drug of choice when given intravenously for the treatment of cerebral malaria. On the other hand, it has certain important shortcomings to which attention was directed by the malaria outbreak in Macedonia during the 1914–18 war. Contrary to experience in peacetime conditions in certain of the Colonies, it was found that quinine was unsuccessful as a prophylactic and had little effect in countering the massive infection which prevailed at that time. It failed to produce radical cure, particularly in benign tertian (vivax) malaria, as shown by the numerous relapses which subsequently occurred. Finally, it did not destroy gametocytes of *P. falciparum*, which continued to circulate unaffected even by intensive courses of quinine.

In the last twenty-five years a number of new anti-malarial drugs have been synthesized that are of value

mainly because they have among them a wider range of action than quinine and cover some of the gaps in which quinine is ineffective.

"Plasmoquine" (now called pamaquin) is a relatively poor schizonticide but is active against the sexual forms of *P. falciparum* and against the resting forms of *P. vivax*, which maintain infection between relapses. Unfortunately this action is limited by toxicity, so that the small doses of the drug which can be administered with safety are not always sufficient to kill all these forms. Pamaquin is usually given for radical cure either with quinine or following one of the other schizonticides to be described. This combination of drugs reduces the relapse rate in vivax malaria to about 10%, or roughly one-sixth of what it is when a schizonticide alone is used in treatment. Two other closely related compounds, pentaquine and isopentaquine, have a similar action and no outstanding advantage over pamaquin.

"Atebrin" (renamed quinacrine and finally mepacrine) has schizonticidal properties which parallel closely those of quinine. It is relatively tasteless, and rarely causes unpleasant symptoms, although, for cosmetic reasons, objection may be taken to the yellow coloration of the skin which it produces on prolonged administration. Its outstanding action in suppression will be mentioned later.

The compound now known as chloroquine (synonyms, "resochin" and "aralen"), first produced in Germany and resynthesized in U.S.A. after being "captured" in North Africa, has proved of great efficiency both in treatment and in suppression.

Finally, the British product, "paludrine" (proguanil), gave promise of outclassing all other antimalarials. In routine use it has proved to have certain drawbacks, the most serious of which is a tendency to induce the emergence of drug-resistant variants of the parasite. Should these forms become widely distributed, the use of proguanil will be greatly restricted, if not contraindicated. Its schizonticidal properties in falciparum infection are not outstanding, but in vivax relapses in a premunized community a single dose effects a cure. Its most important application is as a prophylactic or suppressant.

With these compounds, selected in accordance with the circumstances of the case, it is now possible to attack effectively every stage of the parasite with the exception of the resting or tissue forms of *P. vivax*, and even these are partially sensitive to the pamaquin series.

Drug Suppression

Probably the most monumental work on malaria in recent years is to be found in the investigations of Fairley and his colleagues which were carried out at Cairns, in Australia, during the 1939–45 war. By means of experiments with controlled infections in human volunteers irrefutable evidence was produced on the problems of causal prophylaxis and suppression. Quinine was shown to be inadequate against massive infecting doses of sporozoites, while mepacrine gave complete suppression. There can be no doubt that the rigorous application of mepacrine suppression had a vital influence on the course of the campaign in the South-West Pacific, as malarial infections, which might have been expected to rival those of the first war in Macedonia, were negligible.

Later experiments along the same lines showed that chloroquine was also a reliable suppressant and proved that proguanil not only suppressed vivax malaria but was a causal prophylactic against falciparum infection. It is disturbing that recent work by Field suggests that the long-continued administration of proguanil for prophylactic purposes may lead to the emergence of resistant strains, for in certain ways this compound has advantages over the other preparations.

To summarize, it can be claimed that ways and means have been discovered by which, in favourable circumstances, mosquitoes—and hence malaria—can be eradicated; by which infection can be suppressed where eradication is impossible or impracticable; and by which attacks of malaria can be cured where suppression has been faulty or when suppressive drugs are withdrawn. The major problems of malaria are now administrative rather than medical.

Blackwater Fever

The immediate cause of an attack of blackwater fever still remains to be discovered, though its relationship to recurrent falciparum malaria and quinine administration is amply confirmed. However, when the new suppressive drugs are conscientiously used, as they were in the South-West Pacific campaign, the risk of this disease, whatever its cause, is all but eliminated.

Leishmaniasis

Kala-azar

At the beginning of the century kala-azar was known as an ill-defined and very deadly disease which had become prevalent in Assam in the preceding fifteen to twenty years. It has subsequently been recognized in other parts of the world—China, Central Asia, the Mediterranean littoral, and parts of Africa and South America. The human disease has been found to be associated with a canine reservoir of infection in certain countries, and the epidemiology in Southern Sudan suggests that another reservoir may exist in small rodents.

The discovery of the causative parasite, *Leishmania donovani*, made independently by Leishman and Donovan in 1903, led to a prolonged search for the vector, a problem which was not finally solved until 1942. Although direct transmission long remained suspect (for leishmania parasites are found in the faeces and nasal discharge of victims of the disease) the evidence incriminating an insect vector —which ultimately narrowed down, so far as Assam is concerned, to one species of sandfly (*Phlebotomus argentipes*) —was overwhelming. A complete cycle of development was found in this insect when it was fed on kala-azar cases, yet numerous attempts to transmit the disease by its bite to susceptible animals (hamsters and mice) and man were for many years unavailing. Success came later in a surprising way when it was discovered by Shortt and his colleagues that a minor modification in the feeding of the infected sandfly—a diet of fruit juice (raisins) instead of blood after the first blood-feed from the kala-azar patient —made it possible for the insect to transmit the disease to experimental animals and human volunteers.

Antimony has been found to have a powerful action on the leishmania parasite. First administered as tartar emetic, it is now given with better results in the form of quinquevalent compounds, of which the most effective are "neostibosan," "urea stibamine," and quinquevalent sodium antimony gluconate ("solustibosan," "pentostam"). With these drugs a high percentage of cures can be obtained, the last-mentioned in particular being successful even in the very refractory type of the disease which occurs in Sudan.

Good results have been given by certain of the diamidines, particularly stilbamidine, but this preparation has fallen into disfavour because of its tendency to cause late cranial nerve lesions.

Oriental Sore

Parasites first described in Russia in 1898 as the cause of oriental sore were subsequently identified as Leishman–Donovan bodies, and their relationship to the disease was confirmed by experimental transmission. As in the case of kala-azar, the parasites have been shown to be carried by the sandfly and, where local treatment fails, antimonial preparations given intravenously effect a cure. Here, too, some evidence has been adduced to incriminate a rodent reservoir of infection.

Trypanosomiasis

Nothing was known of the aetiology of sleeping sickness in 1900, and the best suggestion that Manson could make at that time was that it might be associated with infection with *Filaria perstans*. The discovery of the trypanosome in the blood and cerebrospinal fluid, and its incrimination as the cause of sleeping sickness, was made in the early years of the century, and was followed by the gradual unravelling of the details of its development in and transmission by the tsetse fly.

The campaign to control the more chronic and widespread sleeping sickness of West Africa (which is also found elsewhere throughout the tsetse belt) has been unremitting. The provision of centres for mass treatment has played an important part, both in giving relief to sufferers and in reducing the reservoir of infection. In the earlier years of the century tartar emetic was used with considerable success, but this has been replaced with more potent synthetic preparations, of which suramin ("antrypol," "Bayer 205") and, more recently, pentamidine are the most favoured. Unfortunately, these compounds do not pass the blood–brain barrier and hence have proved of little value in the treatment of advanced cases in which the trypanosomes have reached the nervous system. For such late cases arsenical compounds, of which tryparsamide is regarded as the most effective, have been used. Tryparsamide, in turn, has a serious fault. On prolonged administration it tends to give rise to drug-resistant strains of the trypanosome against which it is inactive. These strains retain their resistance in cyclical transmission through the tsetse fly. No satisfactory preparation which will attack the trypanosomes in both blood and central nervous system, and which will not produce resistant strains, has yet been found.

In addition to mass treatment, the extermination of the vector has developed as an essential part of prophylaxis. A study of the oecology of *Glossina palpalis* and *G. tachinoides*, which transmit *Trypanosoma gambiense*, has shown that these flies breed only within a few yards of water and cannot survive in the absence of suitable shade and humidity. In consequence they can be controlled by cutting down all trees within a few yards of streams near villages and by making wider protective clearings at fords and other spots where man habitually approaches the water. An alternative method of "selective clearance" has been tried in Gold Coast territory. It was observed that the requisite "microclimate" for breeding could be provided only by certain species of trees which have a patchy distribution. By training native gangs in the recognition of the types of tree in question and by setting them to cut these out over an entire system of river and tributaries a dramatic reduction in tsetse flies and sleeping sickness has been effected in certain areas.

In Nigeria the removal of entire villages from highly endemic areas which cannot be economically cleared of flies to a specially prepared fly-free tract of country has been carried out with success under the "Anchau Corridor" scheme. The new homes are in the form of hygienic model villages and settlements, with a suitably organized scheme of local government and educational facilities designed to improve the general standard of living. This experiment has important implications other than its success in eradicating sleeping sickness, and is being watched with much interest.

Drug prophylaxis in trypanosomiasis has been tried in recent years, particularly in Belgian Congo, and pentamidine has proved to be the most successful compound for this purpose, though suramin has also been used with good results. It is claimed that a single dose of pentamidine will give protection for six months, a claim which at first sight appears extravagant but which is being substantiated by a growing mass of figures. If finally confirmed, this constitutes a most important advance.

The control of Rhodesian sleeping sickness has proved more difficult because of the scattered breeding-places and different habits of the vectors, *G. morsitans*, *G. swinnertoni*, and other less important species. By increasing the human population per square mile beyond a certain density and reducing or eliminating the big game (on which the flies feed), conditions are produced in which the flies cannot survive; but such a method has a restricted application. Discriminative clearing of trees and other biological methods of control have been successfully used, and spraying D.D.T. from aircraft, though very expensive, has also given good results in fly destruction.

No easy road to the solution of the trypanosomiasis problem has been discovered. By the application of the methods which have been outlined, a notable degree of control has nevertheless been established, and further progress may be confidently anticipated.

In South America, *T. cruzi* has been shown to be the cause of *Chaga's disease*, an acute febrile condition which if not fatal becomes chronic, with cardiac complications. It is carried by certain flying bugs of the genus *Triatoma*, and is found in various wild mammals. In the conditions which exist in the villages where the disease occurs little can be done to prevent it. No satisfactory cure is yet known.

Dysentery

Differentiation of amoebic and bacillary dysentery was vague fifty years ago. The former was recognized, but, although Shiga had identified the organism which has been named after him, the significance of his discovery was not appreciated for some time. Many other types of dysentery bacilli have subsequently been found, and it is probable that the majority are now known. The differential diagnosis of amoebic and bacillary dysentery and the isolation and identification of the different types of dysentery bacilli are now matters of laboratory routine.

Despite much research a great deal has still to be learnt about the aetiology of amoebic dysentery, for which the amoeba does not appear to be solely responsible. The symptomless cyst-passer or carrier, who can be found in appreciable numbers in countries, such as Britain, where overt amoebiasis is very rare, remains an enigma. Theories which postulate non-pathogenic races of amoebae or suggest the synergic action of certain species of bacteria with the amoeba, have been actively explored but still lack factual confirmation.

A notable advance in the treatment of amoebic infection —whether as dysenteric ulceration of the bowel or as tropical abscess in the liver—was the identification of emetine as the active principle of ipecacuanha. With this alkaloid in one form or another it became possible to cure

most cases of amoebiasis, though in old-standing infections with much secondary bacterial invasion (as seen in patients invalided from the Burma campaign) adjuvant treatment with penicillin and a slowly absorbed sulphonamide, sulphasuxidine, has been found of much advantage. Certain other compounds, such as the oxyquinolines ("yatren" and chiniofon), carbarsone (an organic arsenical), and "diodoquin," have been shown to be useful in some cases, while the recently discovered antibiotic "aureomycin" is also claimed to be effective. Despite all efforts to break new ground it has to be confessed that emetine is still unrivalled.

Once bacillary and amoebic dysentery were clearly differentiated it became evident that the former was both more common and epidemiologically more important than the latter, a fact well demonstrated by the crippling epidemics in Gallipoli and Macedonia during the 1914–18 war. The approved treatment at that time—saline purgatives—was of doubtful value, and antitoxin for Shiga infection had no more than a temporary effect. With the advent of sulphonamide treatment (sulphaguanidine was the first preparation used, being tried in the Middle East Force late in 1940) the picture changed dramatically. Almost without exception immediate improvement followed the administration of this compound, and when adequate supplies became available bacillary dysentery, though it still had a high nuisance value, ceased to be a disease of major importance. Subsequent trials showed that all the sulphonamide drugs were effective to a greater or lesser degree. Sulphaguanidine has, however, remained the preparation of choice with British practitioners, as it rarely produces any unpleasant side-effects and is safe to use in tropical climates because, unlike certain others of the series, it has no tendency to crystallize out in the urinary tubules.

With the exception of antitoxin, which has still a place in acute Shiga infections coming for treatment late in the disease, all other methods of treatment formerly in vogue have been given up in favour of sulphonamides. The use of these drugs in bacillary dysentery is one of the major advances in tropical medicine, the advantages of which can be fully appreciated only by those who had experience of dysentery in the days before they were available.

Plague

The development of the plague bacillus in the rat flea and the role of this insect in transmitting plague between animal and man was first suspected and finally confirmed in the early years of this century. On the basis of this discovery, destruction of rats became a standard method of preventing plague. This has been successful where carried out with thoroughness, but in the insanitary conditions which prevail in native villages the results have often been disappointing. Of recent years flea destruction with D.D.T. powder blown into rat-holes or thickly applied to captured and subsequently released rats has been attempted with apparently good results.

Considerable attention has been devoted to sylvatic plague, which is enzootic in various small rodents over wide areas in different parts of the world and is a persistent source of danger.

Vaccines for immunization against plague, which have been developed from the original Haffkine vaccine, have been widely used with encouraging results. Two doses at an interval of ten days are needed to give good immunity, but such a policy is difficult to pursue in epidemic conditions, and it is more usual to adopt the unsatisfactory practice of giving a single large dose. Recently this difficulty has been overcome by the use of a living vaccine of non-virulent bacilli, given in the Dutch East Indies and in Madagascar with apparent success. This vaccine has the advantage of being administered in one dose and of causing little reaction, and the disadvantage of deteriorating so rapidly that it can be used only within a limited range of the laboratory where it is prepared. Attempts are now being made to produce a stable dried vaccine which will contain a high percentage of viable organisms when reconstituted.

In the treatment of plague, streptomycin has given promising results, and, to a less extent, so have certain of the sulphonamides. Antiserum and sulphonamides together are good, but unfortunately both streptomycin and serum are too expensive for routine use on a large scale.

Cholera

The cholera vibrio was discovered by Koch in Egypt in 1883, and the spread of the disease by contaminated water and food has long been recognized. Modern methods of sanitation and, in particular, chlorination of water have greatly limited the incidence of cholera. Nevertheless it is still present in endemic form in Central China and Lower Bengal, and from time to time, especially in periods of war and civil unrest, escapes from these boundaries and spreads far afield—witness the outbreak in Egypt in 1947. Prophylactic inoculation with vaccines made from vibrios of the right antigenic type has been shown to give some degree of immunity, but prevention primarily rests on good hygiene. In treatment the replacement of body fluid, preferably with hypertonic saline, was advised by Rogers, and is a life-saving measure when it can be carried out. No specific chemotherapeutic agent has been discovered, and claims made on behalf of the sulphonamides have not been substantiated.

Leprosy

Significant though not dramatic advances have been made in the treatment of leprosy in the course of the last fifty years. Chaulmoogra oil, previously used in the crude state, has been refined and is now given in the form of its ethyl esters or as sodium hydnocarpate. When treatment is started early in the disease beneficial action is usually well marked, though permanent cure is not often achieved.

In the last few years sulphone treatment has been introduced and has proved more effective than anything hitherto tried. The parent compound, diamino-diphenyl sulphone, is active but somewhat toxic and must be given only under careful control. The less toxic but more expensive derivatives "sulphetrone," "promanide" (U.S.A., "promin"), and "diasone" are generally preferred. These drugs are given in comparatively large doses over long periods of time, and during their administration the patient's general health must be carefully maintained. Clinical improvement, especially in the lepromatous form, may be striking, but the patient may not become bacteriologically negative for months or years.

At one time lepers, when recognized as such, were segregated for life. In many countries where reasonable hygienic conditions exist it is now the practice to allow those who have become non-infective to return, under supervision, to their homes and families. This has done much to stop concealment, and more cases are reporting in the early and more curable stages of the disease. Recognition of the fact that leprosy infection is often contracted by the children of leprotic parents has also shaped sociological policy in relation to this disease.

Yellow Fever

In 1900 Reed and his co-workers showed that yellow fever is conveyed by *Aëdes aegypti* and that the infective agent, which is present in the patient's blood only during the first three days of the disease and which can be passed through a Berkefeld filter, undergoes some form of development in the mosquito before the latter is capable of transmitting the disease. *A. aegypti* is a "domestic" mosquito which is comparatively easy to control. By active campaigns and constant vigilance it has been eradicated or reduced to negligible numbers in ports and other urban areas where epidemic yellow fever was wont to occur, with the result that this disease is now of considerable rarity. The last recorded outbreak of importance was in the Nuba Mountain area of Anglo-Egyptian Sudan in 1940.

In South America sporadic cases to which the name of jungle yellow fever was given were found to occur from time to time in forest areas, and with the development of immunity tests it became possible to study this problem more closely both in South America and in Central Africa, where a similar state of affairs was later discovered. Yellow fever was found to be enzootic in certain species of monkeys and to be carried by mosquitoes other than *A. aegypti*. This monkey virus, which is identical with the urban epidemic virus, is transmitted to human beings living in or near the forest. There seems little doubt that jungle yellow fever constitutes the reservoir of infection and is capable of lighting up the disease in epidemic form when introduced by some traveller into a city in which *A. aegypti* is prevalent.

With the development of methods of cultivating the virus in the chick embryo large-scale vaccine production became possible. A stable attenuated strain of virus (the 17D strain) has been used throughout the world for this purpose. The immunity produced by inoculation with this vaccine is of a high order and lasts at least four years.

Air transport has greatly increased the risk of the spread of yellow fever to countries in which it has not previously occurred (particularly India and the Far East). Vaccination of all travellers before they are permitted to pass through endemic areas has eliminated this danger so far as the human carrier is concerned, and thorough disinsectization of aeroplanes has been used to destroy infected mosquitoes which may be casual passengers. The success of these measures, particularly in the disturbed conditions which prevailed during the second world war, reflects favourably on their efficiency.

Dengue and Sandfly (Phlebotomus) Fever

There is little to be said of these two diseases except that the identification of the insect vectors—species of *Aëdes* and *Phlebotomus papatasii* respectively—has made it possible to control their spread. The new insecticides are very useful in eliminating sandflies, which were very difficult to cope with by the older methods.

Scrub Typhus

Certain of the rickettsial fevers are found only in tropical countries, being restricted by the geographical distribution of the vector. Of these the most important is scrub typhus, a disease proved to be conveyed by the bite of the larva of the mite *Trombiculus deliensis*, the reservoir of infection being in certain rodents. This infection has long been known as tsutsugamushi disease in Japan, but was only recently recognized in Malaya. During the 1939–45 war it assumed great importance in the South-East Asia and Burma campaigns, where some thousands of casualties with a high mortality rate caused grave concern. Prophylaxis was attempted by means of mite-repellents and vaccine. Of the former, dibutylphthalate applied by hand to the clothing was ultimately used with great success by Australian troops, and the incidence of scrub typhus was thereby reduced to insignificant figures. A vaccine prepared from the lungs of infected cotton-rats was developed and was ready for trial when Japan collapsed, and the risk of scrub typhus infection became negligible. Thus a bold experiment did not reach its conclusion, and no information, positive or negative, was gained from it.

In the last two years it has been found that the new antibiotics chloramphenicol and aureomycin have a specific action in scrub typhus, reducing the temperature to normal within two days and bringing about a dramatic improvement in other symptoms.

This important disease has therefore been clearly defined. its cause, reservoir host, and vector have been discovered. successful methods for its prevention have been devised. and a cure for the established disease has been found—a record of gratifying completeness.

Helminthic Diseases

Although the life-cycle of the fluke which causes *schistosomiasis* was accurately forecast many years previously, factual proof of the theory was not forthcoming until Japanese workers in 1913 traced the different stages of *Schistosoma japonicum* through a snail and back to the human host. A year later Leiper made similar observations on the Egyptian schistosomes.

This discovery indicated the steps necessary for the prevention of the disease—the avoidance of water contaminated with infective cercariae and, as a long-term policy, the destruction of the snails which act as intermediate host. The former is comparatively easy for the well-to-do, but impossible for the peasant who spends much of his time working on artificially irrigated land.

The eradication of the intermediate host has so far proved an almost insoluble problem. It involves extensive weed clearance and the treatment of streams, canals, and pools with a molluscicide, copper sulphate being the most effective yet discovered. Reasonably good results have been obtained in areas where the problem is a localized one, as in the Fayoum oasis in Egypt, but it is impossible to treat successfully a vast tract such as the Delta of the Nile, where irrigation canals and infected snails are ubiquitous.

In the treatment of schistosomiasis tervalent antimonial preparations have been found to give fairly good results. A long course is necessary and side-effects are unpleasant. Nevertheless, mass treatment centres, at which tartar emetic is administered as a routine, have been widely established in certain heavily infected areas and have been of considerable value in improving the general level of health. A synthesized thiazanthone compound, "miracil D" ("nilodin"), has recently been under trial, with promising results. It is given by mouth.

The schistosomiasis problem remains a formidable one, and constitutes an ominous threat in countries such as Iraq, where extensive new irrigation schemes are planned. Active measures are being taken to combat the disease in those countries where it is prevalent, but no striking degree of success can yet be claimed.

Until a few years ago no drug was known to have any action against *Wuchereria bancrofti*, the nematode which causes *elephantiasis* and allied complaints. Recently Culbertson and his co-workers have shown that certain antimony preparations kill the adult worms. This action

is masked by the fact that the microfilariae are unaffected by the treatment and live out their normal life span, slowly and gradually disappearing over a period of nine months to a year. At a still later date a synthetic piperazine compound, "hetrazan" ("banocide") was found to cause rapid disappearance of microfilariae. It remains to be seen whether or not it kills the adult *W. bancrofti*. Its action on *Loa loa*, the worm which causes Calabar swellings, appears to be definitely proved. "Hetrazan" has, however, failed to kill the adult forms of *Onchocerca volvulus*, although it destroys the microfilariae.

There is still controversy regarding the importance of the moderate or insignificant degrees of *ankylostomiasis* which are common in the natives of many parts of the Tropics. Experimental mass treatment campaigns have been carried out in certain communities, and it is claimed that the results have been beneficial. To maintain the ankylostome-free state is wellnigh impossible in the absence of proper sanitation.

Vitamin-deficiency Diseases

Certain vitamin-deficiency diseases, such as beriberi and pellagra, are usually regarded as tropical diseases because they commonly arise from the dietetic habits of the natives of hot countries. At the beginning of the century vitamins were unknown, and, although Japanese workers claimed to have shown that beriberi was due to a deficiency in dietary nitrogen, this view was not accepted, and Manson expressed the belief that it was a germ disease, the germ residing outside the body, perhaps in the soil, where it distilled a toxin which, when absorbed into the body, produced neuritis. The association of beriberi with the consumption of milled rice was later observed and confirmed, and from this sprang several theories, of which the two principal were (1) that a toxin was produced or was present in overmilled rice which was counteracted by its "antidote" in the discarded millings, and (2) that an essential factor, subsequently identified as vitamin B_1 (aneurin, thiamin), was discarded in the polishings. The latter theory (vitamin B_1 deficiency) is now widely held, yet has not been convincingly confirmed by experiment. The administration of aneurin does not of itself cure beriberi. It acts best when supplemented with a diet rich in first-class protein, particularly if given with yeast, which contains all the known B complex vitamins and possibly some unknown ones as well.

Pellagra occurs mainly, but not solely, in communities in which the staple article of diet is maize. First vitamin B_2 (riboflavin) and then vitamin B_6 (nicotinic acid) were claimed to be the missing elements in the diet responsible for this disease. Neither has proved to be wholly successful in treatment, and here also it has been shown that a generous diet rich in protein is necessary. Considerable evidence has been produced in support of the theory that maize contains a pellagragenic factor which by its toxic action produces the symptoms of this disease.

Sprue

The exact cause of sprue remains unknown in spite of much investigation, and methods of prevention are therefore empirical. Experience in India during the 1939–45 war has shown that long residence in unfavourable surroundings is not an essential part of the aetiology, and also that the disease can occur in men eating full rations and living in a relatively innocuous climate—observations which run counter to previously held theories. There is evidence that the disordered absorption of fats from the bowel is due to defective phosphorylation, and it has been suggested that the latter results from a breakdown of the enzymic systems concerned in the process, which in turn might arise from an altered biosynthesis caused by a change in intestinal flora. This hypothesis has not yet been confirmed by experimental methods.

In treatment the value of a diet rich in protein and low in fat and carbohydrate has been proved, while crude liver extract has improved the blood symptoms and cleared up the mouth and tongue lesions. Folic acid has, on the whole, been disappointing.

Other Diseases

Some of the more important tropical diseases to which no reference has been made, though all have been the subject of much investigation, are the tropical anaemias, enteric and undulant fevers (which are not confined to the Tropics), louse-borne and tick-borne relapsing fever, yaws, tropical skin diseases, and tropical ulcer (a most revolting condition when seen in epidemic form). In most of these the aetiology has been disclosed, and more or less effective methods of treatment are known.

Conclusion

From this brief review it will be seen that the dweller in the Tropics in 1950 faces a very different prospect from his predecessor in 1900. The temporary resident who takes strict precautions can hope to escape infection or, if he should contract a tropical disease, may expect to be cured without suffering from any grave or permanent ill-effects.

Unfortunately, the same cannot always be said of the native population, mainly because of their poverty and "backwardness." An improvement in the general standard of health can be expected only if there is a parallel improvement in economic conditions and in education—better agriculture, better food, better housing, intelligent hygiene, and the many other things which form part of evolving civilization. It is perhaps fair to say that, in tropical medicine, knowledge of the methods of prevention and cure of disease has outstripped its practical application. Even so, the research worker can console himself with the reflection that there is infinitely more still to be discovered than is already known.

". . . For a long time Ross could get no further. He failed to trace the future progress of the flagellum in the mosquito. In the paper which we publish to-day we may have the explanation of his failure. Possibly he was working with the wrong species of mosquito, for now he tells us that at last, in a species of insect which hitherto he had not an opportunity of working with, he has found in certain cells in the stomach wall peculiar pigmented bodies which may turn out to be the maturing form of the extracorporeal or mosquito phase of the malaria parasite. If he has not quite proved that the malaria flagellum or flagellated spore enters a mosquito cell, he has now almost certainly proved, as attested by Mr. Bland Sutton, Dr. Thin, and Dr. Patrick Manson, that a product—melanin—characteristic of the malaria parasite is to be found in certain cells in the walls of the stomach of a certain species of mosquito after it has fed on crescent-containing malaria blood." From a leading article in the *British Medical Journal* of December 18, 1897 (p. 1805), commenting on a paper published in that issue by Surgeon-Major Ronald Ross, I.M.S.

FIFTY YEARS OF RADIOLOGY

BY

S. COCHRANE SHANKS, M.D., F.R.C.P., F.F.R.
Director, X-ray Diagnostic Department, University College Hospital

When one attempts to survey the achievement of diagnostic and therapeutic radiology in the past half-century it is appropriate to project the story five years back into the nineteenth century, and to consider that late afternoon, so heavy with importance for mankind, of Friday, November 8, 1895. The time of discovery was ripe, for already it was known that cathode rays could excite a fluorescent screen and blacken a photographic plate. Any one of half a dozen physicists might have made the discovery of *x* rays, for all must have been on the verge of it. Indeed, Crookes returned to the makers some photographic plates because they were fogged; fogged, had he but known, by *x* rays emitted during his cathode-ray experiments. If only he had stopped to ask why! And so the questing spirit and the fortune of blind chance together placed the name of Wilhelm Konrad Röntgen on the roll of the immortals of science. Chance decreed that there lay on a near-by bench a platinocyanide screen, and that dusk had fallen during Röntgen's experiments on the cathode rays—dusk that made visible the tell-tale gleam from the screen on the bench in a position beyond the reach of the cathode rays themselves. But the lucky concourse of circumstance was unavailing without the inquiring mind. Crookes, absorbed in another research, failed to ask why. Röntgen did ask, and humanity was in his debt thereafter.

Röntgen made his classic observation on November 8, and his first paper, "Uber eine neue Art von Strahlen," appeared only seven weeks later, on December 28. It seems that he realized the urgency in staking his claim to the discovery; that he knew many of his colleagues must be hard upon his heels. And in those seven weeks he had elucidated in a remarkable way the properties of *x* rays; their capacity to penetrate substances opaque to light, to affect a photographic plate and a fluorescent screen; that they could not be reflected by a prism or a magnetic field or focused by a lens; and that the opacity of substances to them depended on the density (or atomic weight) of the substance. Thus from that small Ruhmkorff coil and that primitive Hittorf-Crookes tube, in the hands of a great man, has come an entirely new specialty—a method of investigation now so important that one out of every two patients attending hospitals is subjected to it.

Apparatus

The advances in diagnostic radiology in the past half-century would not have been possible without revolutionary improvements in the apparatus used for producing *x* rays. The early workers were immensely handicapped by the primitive feeble machines of the turn of the century. Exposures of 5 to 30 minutes were often necessary to produce any photographic effect on the *x*-ray plate, and *x*-ray burns of the skin nearest the tube were not uncommon, and gave the first warning of the potent dangers of *x* rays. There are certain landmarks in the development of *x*-ray apparatus since 1895. The Wimshurst static machine, with its huge glass case filling up half a room, and its feeble output of 1 mA, rapidly became the first *x*-ray museum piece, and favour returned to the induction coil. Already in 1896, 12-in. (30-cm.) coils were available, and for the next twenty years coils up to 32 in. (80 cm.) were in common use in this country. In 1907 the American "Snook" interrupterless transformer made available a high-voltage current of 50 mA and switched the problem to that of the *x*-ray tube. The gas tubes then in use were rapidly ruined by a current of that magnitude, and the next great advance came when Coolidge in 1913 introduced his hot cathode tube. With this tube relatively high-speed radiography of the chest was possible. Still heavier loading was possible when Bauwers introduced the line-focus tube; and when in 1929 he introduced the spinning target the pattern was set for the modern rotating anode tube with its great output. Ray-proof and shock-proof tubes were soon to follow, and now the modern unit is an instrument of precision, with an output up to 500 mA and a time-switch accurate down to 0.02 second.

It was not until 1920, when Seitz and Wintz, of Erlangen, introduced 200 kV deep therapy in place of the previous 100 kV, that specialized radiotherapy apparatus was developed. Before then radiotherapy was given with diagnostic apparatus, and the Erlangen technique marked the beginning of a new specialty—radiotherapy. The first deep-therapy apparatus gave an output of 2–5 mA at 200 kV. Now the milliamperage may go up to 30 and the voltage to two millions. And beyond that are the betatron, the synchrotron, the linear accelerator, and doubtless further machines with even more astronomical voltages attached to them.

Clinical Radiodiagnosis

The First Five Years

The clinical applications of the new rays followed very quickly on their discovery. The first *x*-ray picture taken for clinical purposes is generally accredited to Campbell Swinton, F.R.S., the date being January 7, 1896. He was a distinguished British electrical engineer who devoted much of his life to scientific research and in 1911 became President of the Röntgen Society (now the British Institute of Radiology), the oldest radiological society in the world. Professor Pupin in the same month took the first radiograph in the United States in a case of multiple gunshot wounds of the hand. The exposure was *one hour*. To reduce this time Pupin tried the effect of interposing a fluorescent screen—the first application of the use of intensifying screens in radiography.

One of the earliest radiographs taken in this country is that shown on page 7 of the special illustrated supplement to this issue. This is the first *x*-ray picture taken of a patient of University College Hospital, by J. Norman Collie, Professor of Organic Chemistry at University College, London. Collie is reputed to have said, "If anyone happens to write an obituary of me, I want two things said: I first discovered neon, and I took the first *x*-rays." Collie was a great Alpine climber, and this statement did appear in his obituary notice in the *Alpine Journal*. The exact date of this picture is not recorded, and so evidence is wanting that it antedates that of Campbell Swinton.

Understandably, the first use of *x* rays was in the detection of opaque foreign bodies. This was quickly followed by localization of foreign bodies. In 1896 Sir James Mackenzie Davidson introduced stereoscopy in localization, and a year later his famous cross-thread method of localization. And in 1898 Sweet introduced his method of localizing metallic fragments in the eye, which has stood the test of years and is still used to-day. Hard upon this came the radiological demonstration of fractures, followed during

the next ten years by the use of *x* rays in the investigation of tuberculous and other forms of arthritis, of constitutional diseases of bone, and of bony tumours.

The relative ease with which the early primitive apparatus revealed opaque foreign bodies soon led to the successful detection of urinary calculi. John Macintyre, an aural surgeon of Glasgow and an early and enthusiastic *x*-ray worker, was, in 1896, the first to show a renal stone in a radiograph. His classic experiments a year later on *x*-ray cinematography of the frog's leg are quoted by all who write on that subject, notably by Russell Reynolds, who later did so much to advance this subject. In spite of the observations of F. H. Williams on the *x*-ray investigation of thoracic disease in 1897, and the historic experiments of Cannon with bismuth in the alimentary canal in 1898, radiology at the beginning of the century meant in the main foreign bodies, fractures, and urinary stones. An interesting picture of the state of radiology at this time is given in an article by Sir James Mackenzie Davidson. Mackenzie Davidson was one of the great figures in early British radiology. Born of Scottish parents in Buenos Aires, he received his medical education in Edinburgh, Aberdeen, and London. He was in turn assistant to the Professor of Surgery at Aberdeen University, and then Lecturer in Ophthalmology in the same University. He came to London in 1897 as surgeon to the Röntgen Ray Department at Moorfields. This stimulated his interest in localization of foreign bodies, especially in the eye. Shortly afterwards he became radiologist to the *X*-ray Department at Charing Cross Hospital, an appointment he held till his death in 1919.

In the third edition of Quain's *Dictionary of Medicine*, a volume of 1,892 pages published in 1902, there is a section by Mackenzie Davidson entitled "Röntgen or *X* Rays." This short account, of three pages only, can be regarded as the summation of knowledge on the subject at that time. After describing the properties of *x* rays, he states that "the great practical importance of these rays is their utility in medicine and surgery. So far they seem to serve no useful purpose in any other domain."

The picture of diagnostic radiology that he gives us is one in which fractures and urinary calculi are demonstrable, foreign bodies accurately localized, and stereoscopic pictures a commonplace. For the latter he recommends a cassette tunnel covered with "parchment such as is used in the best drums." For renal stones the exposures had to be so long that he devised an automatic cut-out which, placed on the patient's chest, switched on the current in full inspiration and switched off when the patient let go. The patient held his breath for 20–30 seconds at a time, and the method avoided respiratory movement of the kidney during the 1–2-minute exposures. Other uses were, however, beginning to appear. Mackenzie Davidson had already made and used intra-oral dental films. Of aneurysms of the aorta he noted that they produced "mediastinal projections which pulsate." He remarked that tumours of the lung produced a darker shadow than lung or pleural fluid, and he recorded the movements of the diaphragm.

But the abdomen was still a silent area. This is all he says about it: "The abdomen is very difficult to examine by *x* rays. With the exception of gaseous distension of the stomach, renal calculi, and foreign bodies, which can be detected, little information can be obtained." This was to remain true for many years after it was written.

In this article are noted the beginnings of radiotherapy. Already lupus had been treated successfully—the dread late sequelae were then unknown—and rodent ulcer had been cured. Epilation of superfluous hair had been effected, again without knowledge of the inevitable sequelae. At this early stage, however, something was known of the dangers of *x* rays, and *x*-ray burns and ulcers were on record. Indeed, many workers had become severely affected by the end of 1896, and one of Edison's assistants, Clarence Dally, was the first of a long list of *x*-ray martyrs, dying of cancer secondary to severe *x*-ray dermatitis.

1900–10 Decade

This period was mainly concerned with refinements in existing *x*-ray techniques, extensions in chest radiography, and the beginnings of the radiology of the gastro-intestinal tract. An excellent picture of the achievements of radiology in the middle of this decade is given in a special number of the *Practitioner* published in 1906, and entitled "*X*-rays in Diagnosis." Of the eleven articles, five were written by men who were later to become famous in British radiology—namely, W. Ironside Bruce, R. Higham Cooper, Sir Archibald Douglas Reid, Edward W. H. Shenton, and John Hall-Edwards. It is of interest that in this volume, purporting to cover the field of *x*-ray diagnosis in 1906, there are articles on bones and joints, two on localization of foreign bodies, one on the lungs, and one on the urinary tract; but none on the gastro-intestinal tract. Peristalsis and the long exposures then necessary combined to prevent satisfactory *x*-ray examination of the stomach or intestines. But this was soon to follow.

In the article on the *x*-ray diagnosis of lung disease David Lawson, senior physician to Banchory Sanatorium, indicates how much was known of chest radiology as early as 1905. The fluoroscopic appearances of hydropneumothorax were already known, including the tilting of the fluid level and rippling thereof on movement. Tuberculous cavities were clearly recognizable, as were pleural effusions. Quite a point is made in that article of the fact that the diaphragm moves up and down on respiration. Hugh Walsham, of the London Hospital, was the first to note this and disprove the previous teaching by physiologists that the diaphragmatic movements were those of lateral contraction and expansion towards the central tendon.

Hard upon this time came the turn of the alimentary tract. Rieder had already in 1904 published his comprehensive monograph in the *Fortschritte*, "Beitrage zur Topographie des Magendarmkanales," and soon after there came the observations of Pancoast, of Holzknecht, and of Pfahler. A. E. Barclay in Manchester, Gregory Cole in the U.S.A., and Haudek in Germany were prominent in founding the new branch of gastro-intestinal radiology. Haudek was the first to describe the niche of gastric ulcer, the barium-filled ulcer crater; while Cole preached the importance of the direct sign in duodenal ulcer.

The Second Decade

In the years immediately before the first world war *x*-ray departments were still primitive and the volume of work in them small. I clerked in a medical ward in the Western Infirmary, Glasgow, in 1913, and in the two wards of the unit did not see a single stomach *x*-rayed in six months. This is noteworthy, since this unit specialized in gastro-enterology; and the detection of peptic ulcer and gastric carcinoma depended on the anamnesis, the stomach-tube (a good stout one, half an inch (1.25 cm.) thick), and the guaiac test for occult blood. In those days the diagnosis depended not on the filling defect or the niche but on sarcinae, the Boas-Oppler bacillus, and Uffelmann's test for lactic acid—all from the

gastric washings. A house-surgeoncy two years later proved little more fruitful: a few Colles's and Pott's fractures demonstrated in an *x*-ray plate and one renal stone. During that resident post I assisted at the amputation of a leg for tuberculosis of the ankle in a 12-year-old boy; but no *x*-ray picture was taken before the limb was lopped off, nor dared anyone (save the wretched child) question the surgeon's decision that off it must come. But in truth, save for fractures of the limbs, *x*-ray pictures in those days were too often of little help. Frequently have *x*-ray departments been accused of producing pictures of a November fog. In 1913 such effects were the rule rather than the exception.

Then came the 1914–18 war, and the whole *x*-ray bias turned to foreign bodies, compound fractures, and gas gangrene. Surgeons demanded that shrapnel should be accurately localized even after the wound had healed, and radiologists responded *en masse* with a host of methods of localization—nearly all variants of the simple triangulation method. There are said to be several hundreds of them. An interesting hangover from this 1914 passion for localization projected itself into the second world war, when the Emergency Medical Service equipped all its hospitals with an admirable *x*-ray device for localizing foreign bodies, which, so far as I can gather, hardly anyone ever used.

The Third Decade

The first world war ended, and peace again came to the radiologists. Peace, for little then was expected of them. Seniors who, like myself, are immersed in the turmoil that is the modern *x*-ray department will remember the gentle tempo of the departments of old. To others may I present a picture of my first experience of radiology, as a postgraduate student at Charing Cross Hospital under Dr. Ironside Bruce.

The department was a modern one of its day, for its director was an intelligent, forceful Scot who at that time was one of the foremost figures in a rapidly developing specialty. Alas, in three years he was to die of an agranulocytosis, and radiology of the 'twenties to lose one of its most able exponents. His department was up to date in that it was on the top floor of the hospital instead of the more usual basement—one large room and a cupboard that served as a dark room. The staff consisted of Dr. Bruce, a radiographer (both of whom attended on three afternoons a week), and a sister-in-charge. On an average, ten cases were *x*-rayed on each of these three afternoons, consisting of fractures, chests, and urinary tracts, with an occasional barium meal. The *x*-ray diagnosis of chronic appendicitis (whatever that may be) was just coming into vogue, and I noted the guarded phrase "consistent with a chronic appendicular lesion" creeping into the reports. *X*-ray plates were still in use, the largest size being 12 in. by 10 in. (30 by 25 cm.), and the intensifying screen was still something of a novelty. With it the exposure for a barium meal had been brought down to about a second. The equipment consisted of a 16-in. (40-cm.) coil, gas tubes, a canvas-topped couch, and a primitive screening stand without a screen carriage. The screen was held in the observer's hand against the patient's chest or abdomen.

The double-coated *x*-ray film, which was in a few years to supplant the glass plate entirely, became available in 1918, and with its introduction two intensifying screens could be used. This greatly reduced exposure times and improved radiographic contrast. In the early 'twenties the Potter–Bucky diaphragm, first devised in 1916, came into general use, with still greater improvement in contrast.

Contrast Media

The decade beginning in 1920 found radiology possessed of only three contrast media—air, barium (bismuth was even then on the way out), and the simple halogen compounds: air in the lungs, barium sulphate in the alimentary canal, and sodium iodide in ascending urography. These left many silent areas, including the gall-bladder, the bronchi, and the central nervous system. In 1924 Graham and his colleagues successfully explored the first of these territories, and, although the blue dye iodophthalein which they used has now been discarded in favour of the less irritating pheniodol, the physiological mechanism involved in the test remains the same as in the original cholecystography. Even the term "dye" has been extended to pheniodol, and has splashed over into the urinary tract to include the next two contrast media to be considered. In 1929 Von Lichtenberg and Swick published their paper on uroselectan and laid the foundations of modern intravenous urography. Iodoxyl and diodone are now both in the *British Pharmacopoeia*, and the latter bids fair to become the universal contrast medium, since it is harmless to nearly all tissues. Sicard and Forestier introduced lipiodol in 1922, and before many years were past this iodized oil came into extensive use as a contrast medium, in the bronchi, the uterus and tubes, in fistulae and sinuses, and in the spinal canal.

Central Nervous System

The first real attack on the problems of neuro-radiology was made by Dandy, who in 1918 undertook the first deliberate ventriculography. A year later he devised encephalography by introducing air via a lumbar puncture. Air as a contrast medium in the skull was to remain supreme for many years, and, although Egaz Moniz introduced cerebral angiography in 1927, it was not till the present decade that it largely replaced the earlier methods in the investigation of intracranial lesions. It is a pleasant thought that the work in many fields of this distinguished Portuguese professor of medicine has been so fittingly recognized by the award of a Nobel Prize. Moniz used thorotrast. The dangers inherent in its radioactivity are real, and in preference to it diodone is now used exclusively in arteriography in any part of the body. One of its latest uses is in abdominal arteriography. A second or two after its injection into the abdominal aorta pictures may be taken of the opaque blood vessels of the kidneys, suprarenals, spleen, and pelvic viscera. By this method a tumour of the kidney may be revealed by disturbance of the normal vascular pattern.

The Fourth and Fifth Decades

In the fourth decade, as the years swept on to the second world war, diagnostic radiology steadily expanded, new techniques were evolved, and old ones were refined. A measure of this is in the volume of work done in *x*-ray departments, which has since 1920 doubled on an average every five years. A halt was naturally called by the second world war, but at its end the march was again resumed, and the last five years have seen an even greater increase.

In the last decade of this half-century progress in radiological research was at first interrupted by the war, and the preoccupations were those of an army and civilian emergency medical service. With the end of the war there appeared new fields of investigation: cerebral angiography, angiocardiography, diodone arthrography, and radiological studies of the small intestine, all too recently in the minds of readers to require further comment.

Radiotherapy

It is not within my competence, a diagnostician, to discuss in detail the achievements of radiotherapy during the past half-century, massive as they have been. The earliest attempts at radiotherapy were made without any knowledge of the properties of the rays. They were ventures unpiloted by any knowledge of what might come of them. Among those who experimented thus were E. H. Grubbe, of Chicago, who treated a cancer of the breast in January, 1896, Voigt, of Germany, a cancer of the nasopharynx about the same time, and Despeignes, in France, a cancer of the stomach in the same year. Priorities in such haphazard experiments are of little consequence, and the first serious thoughts of radiotherapy were prompted by the skin reactions which all too soon began to show themselves on the hands of *x*-ray workers. In the year 1896 Bowles and Crocker, in Great Britain, and Feichenfeld, in Germany, expressed the view that the skin reactions were due to *x* rays and not to cathode rays, ultra-violet rays, electro-magnetic fields, heat, or other agent. Crocker, in the *British Medical Journal* of January 8, 1897 (p. 8), published a case, with coloured illustrations, of a severe dermatitis from exposure to *x* rays. Very soon a wealth of clinical and histological information was available about the acute and chronic stages of *x*-ray dermatitis, including epilation.

Radiotherapy in Dermatology

It was inevitable that with this knowledge workers would soon try to use *x* rays therapeutically, and it seems that the credit for the first logical experiment, based on knowledge of the biological action of the rays, should go to Leopold Freund, of Vienna. He treated an extensive and disfiguring hairy naevus in a little girl, with the object of removing the hair. The exposures totalled to 42 hours, and epilation began in seven days, followed in due course by extensive ulceration, which required several excisions. Five years later there was still an ulcer present. Soon after this there came a spate of reports on radiotherapy of skin lesions, benign and malignant, and the first dramatic successes in the radiotherapy of malignant disease were in skin cancers.

Many of the pioneers of radiotherapy were dermatologists. Among them there stand out such names as Colcott Fox, Morris, Dore, Sequeira, Adamson, and Macleod in this country, Sabouraud, Noiré, Wickham, and Degrais, in France, and, in America, Pusey and, later, MacKee. MacKee points out that the first wave of optimism in skin radiotherapy was succeeded by one of pessimism, prompted by the increasing numbers of *x*-ray burns resulting from treatment and by the lack of any means of measuring dosage. Sabouraud and Noiré restored the balance when they introduced the pastille and so established a unit of dosage in superficial *x*-ray therapy.

At the beginning of the century ringworm and favus of the scalp were common diseases and their cure was difficult. *X*-ray epilation, if complete, was soon found to be effective as a cure. Schiff and Freund, Kienböck, Sabouraud, and others reported some successes and many failures. Then Kienböck published his five-area technique in 1907, and this, as modified by Adamson two years later, is the basis of *x*-ray epilation of the scalp to this day. The Sabouraud pastille, although a valuable rough measure of dosage, had too great a variation to be really satisfactory, and MacKee introduced his "electrical constants" technique of dosage, made possible by the use of modern transformers and hot cathode tubes. This is the method still used in skin radiotherapy, with the added safeguard of periodic calibration of the apparatus by the ionization dosimeter.

Radium Therapy

This may be said to have started with the famous Becquerel burn. This great French scientist, the discoverer of the radioactivity of uranium, sustained a burn on the skin of his abdomen by carrying radium in his waistcoat pocket. Pierre Curie produced experimentally a similar burn on his own arm. The French dermatologist, Besnier, of prurigo fame, recognized the lesion as similar to an *x*-ray burn, and suggested that radium might be used therapeutically. Acting on this suggestion, Danlos, of the Hôpital St. Louis, began to treat benign and malignant skin lesions, with some limited success. This was carried out by a radium plaque. For irradiation of deeper structures radium needles were devised, and later the radium "bomb," or teleradium therapy.

The first to use radium *en masse* as a bomb was Regaud, in Paris. There soon followed him Sluys and Murdoch in Brussels, Douglas Quick and Janeways at the Memorial Hospital, New York, and Stanford Cade at Westminster Hospital. Another early worker in this field was Howard Pinch, the first director of the Radium Institute of London.

Deep X-ray Therapy

By 1902, attempts were being made to treat deeper neoplasms—particularly in the breast. For the next two decades minor improvements occurred in the treatment of malignant disease, with increasing knowledge and improved apparatus. In 1920 the Erlangen technique, with kilovoltages of 200, introduced a new conception into the treatment of deep-seated growths: radical radiotherapy with the object of effecting a cure. If that were impossible by reason of the clinical stage of the growth there remained what had previously been available—palliative radiotherapy.

Although the massive single-dose technique of Seitz and Wintz was soon to prove so dangerous that it was discarded in favour of the split-dose technique, it was the starting point of notable advances. Regaud, working with radium, evolved the extended technique of small doses daily over long periods. Pfahler adapted this radium technique for *x* rays in his well-known saturation method. In 1930 Coutard added to these extended techniques the principle of heavy filtration, which greatly improved the depth dose relative to that on the skin. These new techniques were eagerly developed in Great Britain. R. Morton brought the Erlangen technique to London, and gradually there was born in Great Britain a new specialty—radiotherapy.

Diagnostic radiologists were too immersed in their proper subject to have time for the new radiotherapy, and there sprang up in this country radiotherapy centres that were to lead the world, and still do so to this day. Finzi at St. Bartholomew's, Douglas Webster and, later, B. W. Windeyer at the Middlesex, Stanford Cade and Allchin at Westminster; these in London were among those who started the "new look" in radiotherapy; while in the provinces Ralston Paterson had begun to make the Holt-Christie Institute of Manchester one of the most famous radiotherapy centres in the world. It is not without reason that he has been chosen as president of the next International Congress of Radiology, to be held in London next summer.

Any account of the history of radiotherapy, however brief, should have some mention of the great contributions

made by the hospital physicists. It is they who have made possible the scientific accuracy in dosage and beam direction that obtains to-day; and now their work is extending to *x*-ray diagnostic problems and to the great new field of radioactive isotopes in medical research and treatment. Names that deserve honourable mention as pioneers in this country are Professors Russ, Hopwood, and Mayneord.

Radiological Education

It became clear at the end of the first world war that something would have to be done to train radiologists to serve the expanding specialty. British radiologists took the lead in this, and the efforts of A. E. Barclay, Robert Knox, Stanley Melville, Sidney Russ, E. P. Cumberbatch, and others resulted in the institution of the Cambridge Diploma of Radiology and Medical Electricity, the first of its kind in the world. Since then many others have been established, and, indeed, the original D.M.R.E. of Cambridge is no more; but to the foresight of these men is due the comprehensive system of radiological education now extant in many centres in Great Britain. That radiology in both its branches is worthy of academic training is now recognized in the appointment of a number of professors of radiology in British universities; still too few, but a good beginning.

And What of the Future?

In radiodiagnosis there are new fields imminently presenting. The liver, spleen, and pancreas are still silent areas, but already there are hopes of a contrast medium suitable for hepato-lienography. Placentography is also well within the horizon. But even if all these silent areas are explored, and their gross morbid anatomy laid bare, there remains a great new field, the radiological study of function. At the present time, when we screen a barium meal, we see in a glass darkly. Not until we come to view the still life of the resulting radiographs do we study detail. But if we could intensify the screen image to the same brilliance as that with which we view the *x*-ray film how much could we learn. The changing picture of the bulb in duodenal ulcer, the peristaltic cycle of the kidney and ureter, these could be cinematographed and studied at leisure, if only we could make the fluorescent screen image bright enough; while to the cardiac cycle could be applied slow-motion cinematography. Research work is already beginning on this, especially using the techniques of television. If these researches are fruitful, new vistas of radiological investigation open before us.

In radiotherapy, in spite of all the improvements in apparatus and advances in technique and all the achievements of surgery, the great majority of cancers still kill the patient. It is a melancholy fact that although nearly all cancers can be palliated and some so treated as to be held at bay for a time, only four types can be classed as curable: cancer of the breast, the skin, the mouth, and the uterus. At least it can be claimed for radiotherapy that it is the method of choice in the last three. The real cure of cancer is yet to come. In the meantime the field for radiotherapy is increasing, and there is every expectation that the new techniques, using voltages of 2–20 mev., will brighten the prospects of many more who are afflicted with this dread disease.

In conclusion the final words of Mackenzie Davidson's article in 1902 are still appropriate: "That the *x* rays have been of immense value to medical service is unquestionable. It is only a short time since they have been discovered, and we are yet only imperfectly realizing their possibilities."

FIFTY YEARS OF PUBLIC HEALTH LEGISLATION

BY

Sir ARTHUR S. MacNALTY, K.C.B., M.D., F.R.C.P. F.R.C.S.

Formerly Chief Medical Officer of the Ministry of Health

Legislation in public health is of ancient origin. One has only to mention that compendium of sanitary law, the Book of Leviticus, and the Hammurabi Code of Assyria to make this plain. In England the first Sanitary Act was passed by Parliament at Cambridge in 1388, and the reign of Henry VIII produced the Plague edicts for the control of plague and the sweating sickness.

Modern legislation on the subject dates from the Public Health Act of 1848, which first provided a central authority, the General Board of Health. But it must be noted from the outset that British legislation does not of itself initiate public health reforms, nor does it necessarily reflect completely the progress that has been effected. It is only when certain methods have been tried and evaluated, or when scientific discoveries have been made and experimentally applied, that Bills are introduced and Acts passed by Parliament to give these reforms the sanction of law. For the most part, therefore, legislation in public health is a legal ratification of medical advance and not its initiation.

Environmental Hygiene

In the nineteenth century particular attention was devoted by Southwood Smith, Chadwick, Farr, and others to the influence of environment upon health. Simon also advanced the study of environmental hygiene, but his outlook was much wider, and he appreciated the importance of personal infectivity before Pasteur and Koch had founded the science of bacteriology. Under Simon's direction and with the aid of other pioneers in epidemiology, such as were John Snow and William Budd, a vast store of knowledge in environmental hygiene had been collected and applied. This work, surveyed and blessed by the Royal Commission of 1869–71, was expressed in the great Public Health Act of 1875, which consolidated all the previous enactments into a compendious sanitary code. This confirmed the compulsory appointment of medical officers of health by local authorities; it aimed at securing the drainage of houses, the sewerage of towns, the scavenging of streets, the removal of house refuse, wholesome conditions within houses, and the isolation of infectious persons.

During the remaining years of the nineteenth century, although much valuable work was done in public health by the medical department of the Local Government Board, there was little special legislation on the subject. Certain infectious diseases were made compulsorily notifiable in 1889, and other Acts of public health significance were passed. Chief of these was the Local Government Act of 1888, which established the large units of local government, the county councils, and the county borough councils.

By 1900 there was a general decline in mortality and an improvement in national health. "The water-borne diseases became negligible, cholera was abolished, smallpox became rare, and typhus disappeared. Port sanitary administration prevented the admission of plague and pestilence." There was still a regrettable cleavage between preventive and curative medicine, a state of affairs which did not accord with the teaching of Simon, Henry Acland, Burdon-Sanderson, and other enlightened pioneers.

Work of the Social Reformers

The motive power which led to a more comprehensive interpretation of preventive medicine came from without. The last two decades of the nineteenth century and of Queen Victoria's reign were years of social and administrative progress. Side by side with advances in local government and extension of municipal services paid for out of the rates came the rousing efforts of the voluntary reformers. "Settlements," like Toynbee Hall, sprang up in the East End of London; Canon Barnett and his wife worked at practical Christianity in the slums; Charles Booth found that 30% of the London population were living at or below the poverty line: he discussed the problem of public health, the effects upon it of destitution and unemployment, and supplied medical officers of health with new facts, methods, and aims. The Fabian Society, founded in 1884, advocated social development by educational, municipal, and legislative methods, and the historical studies of Sidney and Beatrice Webb contributed largely to the study of social and health reform. There was a Progressive Party in the London County Council, and, in fine, public opinion in favour of health reform was stimulated among all sections of the community and in persons of opposing political views.

"The hour came, but not the man." As the twentieth century dawned there was a great opportunity for a statesman of the calibre of a Disraeli or a Shaftesbury to organize a comprehensive system of preventive and curative medicine for the people of Great Britain which would have met with popular support and acclamation. Despite the pressure from without, the opportunity was not seized. Instead, piecemeal measures were planned to meet the most clamant needs—measures excellent of their kind, but involving cumbrous administration and duplication of effort.

The School Medical Service

The first health service to be established was the School Medical Service. The recruiting figures of the South African War, the physical defects found on medical examination, and the existence of a so-called "C3" population aroused concern. In the Reports of the Royal Commission on Physical Training (Scotland), 1903, and the Interdepartmental Committee on Physical Deterioration, 1904, attention had been drawn to the bad physique of many school-children. Both Reports emphasized the need for a general system of medical inspection and supervision, with the possibility of providing school feeding and medical treatment. The Education (Provision of Meals) Act of 1906 gave power to local education authorities to provide school meals for necessitous children—that is, for children whose physical condition rendered them unfit to take proper advantage of education without such aid—while the Education (Administrative Provisions) Act of 1907 imposed a duty of medical inspection and a power of treatment on the same authorities. From this year dates the Medical Department of the Board of Education and the School Medical Service. Long before its official organization the hygiene of school life was studied by many medical officers of health, teachers, and social workers, and especially, at Bradford, by Dr. James Kerr, who became the first medical officer (Education) of the London County Council. The British Medical Association was active in pressing for the establishment of the School Medical Service.

The subsequent development of this service can be only briefly touched on here. School medical inspection was followed by the treatment of school-children, including medical, dental, and orthopaedic clinics, the sanitation of school premises, systematic physical training, provision of milk and school meals, special education for defective children (blind, crippled, mentally deficient), with the appointment of school doctors and school nurses to visit the homes and to acquaint parents with the importance of seeking medical advice for their children when required. In addition to direct medical results, the teaching of hygiene and the provision of school meals have reformed the physical condition of the children of this land beyond all comparison with the past. "It is an impressive catalogue of great social progress."

National Health Insurance

The need for extension and reorganization of medical services was apparent to all who studied the subject in the early days of the century. Logically, the first step was the reform of the Poor Law; and in 1905 a Royal Commission on the Poor Law was appointed, which issued its majority and minority reports in 1909. It recommended transferring the administration of the Poor Law and its institutions from Boards of Guardians to the councils of the counties and county boroughs. The Commission's reports showed plainly that much of the prevalent poverty and destitution was attributable to sickness and ill-health, and that the existing provision of medical attendance was inadequate.

Mr. John Burns, then President of the Local Government Board, was pressed by his medical advisers to introduce legislation which would not only carry out the recommendations of the Commission but also establish a national health service linking up the public health work of local authorities with specialized and general medical practice. Mr. Burns hesitated in view of the conflicting opinions he received from outside sources, and meanwhile Mr. Lloyd George, the Chancellor of the Exchequer, took effective action.

In 1908 Lloyd George had visited Germany and had been impressed by Bismarck's scheme of national insurance (1880–4). In 1911 he brought in the National Insurance Act, which provided a system of insurance against ill-health for a large section of the working population between certain ages and within certain financial restrictions. Insured workers and their employers paid weekly premiums of equal amount into the insurance fund, which was also subsidized by the State. Administration was undertaken by Approved Societies for sickness, disablement, and maternity benefit, but, in view of medical opposition, Lloyd George altered the Bill to provide for medical control to be exercised by elected *ad hoc* bodies upon which there was due medical representation. Dr. C. Addison, M.P. (now Viscount Addison, K.G.), helped greatly in this matter, and his medical knowledge guided Lloyd George throughout.

Local Insurance Committees were created with medical service subcommittees, while central control was exercised by a new department, the National Health Insurance Commission, under the chairmanship of a Civil Servant, Sir Robert Morant. The chief medical adviser was Sir James Smith Whitaker, the former secretary of the British Medical Association. The Act was brought into operation in 1912 after much controversy and both lay and medical opposition. On January 3, 1913, 10,000 medical practitioners had accepted the terms and 12,000,000 insured persons were enrolled. Twenty-five years later there were more than 15,400,000 insured persons entitled to benefit, about half of whom claimed benefit annually, and there were over 16,000 medical practitioners engaged in this health service. The Act was amended in 1913, 1918, 1920,

1922, 1924 (consolidated), 1928, 1932, 1934, and 1936 (consolidated).

The defects of the National Insurance Act were: (1) although entitled "An Act to provide against loss of health and for the prevention and cure of sickness," it was not adequately associated with the public health work of local authorities; (2) it did not provide for the dependants (wives and children) of insured persons; and (3) it did not provide specialist treatment. Why were these defects not remedied? Economy after one world war and expenditure in view of the second were the explanations given.

On the other hand, the usefulness of the Act is now generally admitted. The institution of medical benefit was of primary importance in confirming the role of the medical practitioner as the first line of defence in combating disease. It provided a means by which the industrial workers of this country had free choice of doctor and ready access to medical advice and treatment.

From 1937 to 1939 the National Health Insurance Scheme also provided for the postgraduate instruction ("refresher courses") of insurance medical practitioners at the chief university centres, the fees and expenses, including the provision of a locumtenent, being defrayed out of national funds.

The Medical Research Council

The National Insurance Act (Sec. 16 (2)) provided that one penny for each insured person might be set aside for the purposes of medical research—a sum estimated to be about £57,000 per annum. A committee under the chairmanship of Lord Moulton, F.R.S., consisting of medical and scientific experts and lay representatives, was appointed to organize this important work.

Through the knowledge, enthusiasm, and energy of the first secretary, Sir Walter Fletcher, a National Institute for Medical Research was established at Hampstead with a distinguished staff. Fletcher made the National Institute with its specialized researches the headquarters, while the Medical Research Committee promoted and co-ordinated medical research throughout the United Kingdom. This benevolent direction was secured through grants by the Committee in aid of "research units" and individual researches in British laboratories. It was exercised by special committees of experts. The Committee was at first attached to the Insurance Commission, and was later, in 1920, constituted as the Medical Research Council, a special committee of the Privy Council. Its income is now derived from an annual Treasury grant. Fletcher established national medical research on secure foundations, and under his successor, Sir Edward Mellanby, it has further advanced and promoted knowledge.

The Tuberculosis and Venereal Diseases Services

Another great service that derived from the National Insurance Act was the Tuberculosis Service. The Act dealt as regards tuberculosis in insured persons with (*a*) treatment; (*b*) erection of sanatoria and other institutions; (*c*) research; and (*d*) education. It was open to the obvious criticism that only insured persons in the community received specialized treatment for tuberculosis, and that the measure was not one of general public health. The Government met this criticism by appointing a Departmental Committee, under the chairmanship of Lord Astor, to report upon a general policy. The committee issued an interim report in 1912 and a final report in 1913.

The State, through Royal Commissions, epidemiological investigations, and a special report on sanatoria had for many years shown its interest in the problem of tuberculosis. Sir Robert Philip's pioneer work in the tuberculosis dispensary at Edinburgh and the establishment of hospitals like the Brompton Hospital and sanatoria like Frimley and Midhurst, together with much other voluntary work, had long indicated concern at the ravages of the disease and revealed methods of attack. Scotland had regarded pulmonary tuberculosis as a notifiable disease in 1897 (Public Health (Scotland) Act). In 1912 the Local Government Board, which had approached the subject by successive stages, made an order extending compulsory notification to cases of all forms of tuberculosis.

The complete scheme for the prevention, detection, and treatment of tuberculosis adopted by the Local Government Board was virtually that recommended by the Departmental Committee. It comprised: (1) the medical officer of health of a county council or county borough as chief administrative officer; (2) tuberculosis medical officers appointed by the local authorities; (3) dispensaries (including a system of health visiting); (4) sanatoria for early cases; and (5) hospitals for intermediate and advanced cases. Insured persons suffering from tuberculosis might be placed on domiciliary treatment (Sec. 16 (1) (b) of the National Health Insurance Act). The Local Government Board, and later the Ministry of Health, acted as a sanctioning, advisory, and subsidizing body. For Wales, tuberculosis work was done on similar lines by the Welsh National Memorial Association. For Scotland, supervision was exercised by the Scottish Board of Health. Legislation concerning powers and duties regarding the treatment of tuberculosis was contained in the Public Health (Tuberculosis) Act, 1921, the Public Health (Tuberculosis) Regulations, 1930, and in Sections 171–175 of the Public Health Act, 1936.

This comprehensive service must have exercised a most beneficial influence upon the decline of tuberculosis. In 1911, immediately before the setting up of the national scheme, there were in England and Wales 38,422 deaths from tuberculosis of the respiratory system; in 1938 the deaths had declined to 21,930. The diminutions in the deaths from other forms of tuberculosis (bone and joint disease, meningitis, glandular disease) were even more remarkable. In England and Wales, in 1911, these deaths numbered 14,698; in 1938 they had fallen to 4,426. The prevention of contact infection, the increased pasteurization of milk, earlier ascertainment, and skilled surgical treatment all no doubt had their effect.

The incidence and dire effects of venereal diseases were considered by a Royal Commission, which reported in 1914 and 1916. Regulations were issued by the Local Government Board in 1916 making counties and county boroughs responsible for a venereal diseases health service, with an Exchequer grant of 75% of the total cost of approved schemes. The Venereal Diseases Act of 1917 implemented these regulations. In this way provision was made for free diagnosis (including pathological examination) and treatment for all classes at special clinics and usually at general hospitals; prohibition of advertisements of remedies and of unqualified practice; and education of the public. The work has met with success, as witness the modern rarity of gummata, thoracic aneurysm, and neurosyphilis, and has been greatly strengthened by the recent discoveries of the therapeutic efficacy of sulphonamide drugs and penicillin and their value in shortening the time of treatment.

Maternity and Child Welfare

Voluntary workers have taken a great part in initiating specialized work in maternity and child welfare. Dr. C. J. Cullingworth and Sir Francis Champneys strenuously

advocated State regulation and training of midwives, and in 1902 the Midwives Act was passed "to secure the better training of midwives and to regulate their practice." For this purpose the Act created the Central Midwives Board under the Privy Council. The Board drew up a set of rules for a course of training for certified midwives, for qualifying examinations (C.M.B.), for registration, conduct, practice, and control, and constituted each county and county borough as a "local supervising authority for midwives" within its area. There was an amending Act in 1918, and the Midwives Act of 1936 set up a comprehensive service of salaried midwives by local authorities.

Every pregnant woman is now able to secure the services of a trained midwife for her confinement, or, if she has engaged a doctor, she is able to obtain a trained midwife to act as maternity nurse and to assist the doctor. Medical practitioners with skilled obstetric experience can be called by midwives in cases of difficulty and danger. Other important features in maternity schemes, based on special investigations and the reports of a Departmental Committee (1929–32), were the satisfactory and sufficient nursing of the mother; maternity centres providing antenatal supervision; maternity homes and hospitals; domestic aid before, at the time of, and after childbirth; maternity benefit and other financial aid; and early notification of births and stillbirths. More attention should also be paid to the provision of post-natal care and gynaecological clinics.

The reduction of puerperal pyrexia by chemotherapy has greatly helped in the campaign. There has been a gratifying decline in the maternal mortality rate per 1,000 live births. For many years this rate averaged 4 per 1,000. Since 1936 it has progressively declined, and in 1946 reached the low figure of 1.17. Extensive national work has been done in the reduction of infantile mortality. The system of child-welfare clinics and milk depots, largely conducted at first by voluntary societies, was made a function of local authorities by the Local Government Board in 1914, the Board being authorized to give grants to the extent of 50% of the authorities' expenditure on approved maternity and child-welfare schemes. The schemes included a health visiting service, nursery schools and infant homes, and accommodation for the sick child in hospitals. The Maternity and Child Welfare Act, 1918, placed this work under the general supervision of the Ministry of Health. The Act was later repealed and included in the Public Health Act, 1936, Sec. 204. Here again the results are most encouraging. In 1900, when voluntary work in child welfare began, the infant death rate for England and Wales was 156: in 1948 it was 34 per 1,000 live births.

The Ministry of Health

In 1918 the Ministry of Health Act was passed by Parliament. This Act created a Ministry of Health and transferred to the Minister the health and Poor Law powers and duties of the Local Government Board; co-ordination with the office of the Registrar-General; the duties and powers of the Insurance Commission; the medical powers and duties of the Board of Education; and the powers of the Privy Council under the Midwives Acts. The high aims of the Ministry of Health have been described as endeavouring "to bring every advance in medical science, every measure calculated to maintain health and to prevent disease to the service of the people and to make health the birthright of every inhabitant of this country."

It has not been unsuccessful in this noble endeavour. But, despite the attainments and work of its medical and lay staff, the Ministry could not have made the progress it has done in national health without the support and co-operation of the medical profession. Leaders of the profession have served on its committees; medical science has given its knowledge and resources; general practitioners have bestowed their time and experience. They have done it selflessly, not looking for fee and reward, but actuated by zeal for the common weal. That is why the campaign for health is such a vital force in Britain to-day.

The Local Government Act of 1929

The Local Government Act of 1929 was a great advance. It associated preventive with curative medicine and made a way for the ending of the Poor Law. The boards of guardians were abolished, their duties, institutions, and resources being transferred to the councils of counties and county boroughs. The Act separated health policy from "pauperism"; a public assistance medical service superseded medical outdoor relief; county councils and county borough councils were empowered to provide general hospitals for the sick and to "appropriate" former Poor Law hospitals also for this purpose; co-operation between local authority and voluntary hospitals was encouraged Annual Exchequer grants-in-aid for individual health services were replaced by "block" grants for a period of years; and county councils were enabled to assist local sanitary authorities. The Act thus brought to fruition that integration of Poor Law and public health services which had been wished for in vain by Simon and recommended by two Royal Commissions (1909 and 1923).

The Public Health Act of 1936

By 1932 there were sixteen statutes relating to public health; that is, as regards environment to such matters as drains and sewers, buildings, water supply, and the abatement of nuisances, and as regards personal hygiene to such matters as the provision of hospitals, maternity centres, etc. A Departmental Committee appointed by the Minister of Health in 1930 considered the consolidation and amendment of these Acts, and drafted a Public Health Bill which with certain amendments became the Public Health Act of 1936. The Act, in addition to the sixteen statutes mentioned, incorporated a number of other enactments related to the public health. Thus the Act also includes the Infectious Disease (Prevention) and (Notification) Acts; the Public Health (Tuberculosis) Act, 1921; the Maternity and Child Welfare Act, 1918; the Nursing Homes Registration Act, 1927; Part I of the Children Act. 1908 (as amended by the Children and Young Persons Act, 1932); the Canal Boats Acts, and a number of individual sections from other Acts, besides repealing certain statutes, such as the Isolation Hospitals Acts, 1893 and 1901. This important Act simplified and rendered easier the administration of public health.

The Metropolitan Asylums Board

The Metropolitan Asylums Board was established in 1867. Over a period of sixty-three years it did valuable work in the provision of mental institutions and fever hospitals. The diseases at first treated in fever hospitals were smallpox, diphtheria, and "fever," a comprehensive term which included cholera, plague, typhoid, typhus, and scarlet fevers. Between the serious outbreak of smallpox in 1870–2 and 1885 nearly 58,000 patients were admitted to the smallpox hospitals of the Board. In order to avoid windborne or aerial infection, smallpox patients for long were isolated on two old wooden battleships, the *Atlas* and the *Endymion*, moored in the Thames, and in hospitals on

lonely parts of its banks. The ships were given up in 1903, when the Joyce Green Smallpox Hospital of 940 beds was erected at Dartford. Later the hospital was used for other diseases.

In 1910 the Board first received cases of measles and whooping-cough in its hospitals. The Board was constituted as a Poor Law authority and was not allowed to accept cases except on the order of a relieving officer based on a certificate from a Poor Law medical officer. This rule was more honoured in the breach than in its observance. The Royal Commission of 1881 recommended that the Board's hospitals for infectious disease should be dissociated from the Poor Law and treated as part of the sanitary arrangements of London. In 1883 the Diseases Prevention (London) Act removed any civil disability formerly attaching to treatment for infectious disease in the Board's hospitals, and in 1889 a Poor Law Act was passed which enabled the Board to admit to its hospitals any person suffering from smallpox, diphtheria, or fever, whether a pauper or not. The Infectious Diseases Notification Act of 1889 steadily increased the number of cases of diphtheria and scarlet fever treated in the Board's hospitals.

Between 1916 and 1919 the Board made provision for the treatment of venereal disease in women and ophthalmia neonatorum in children. In 1925 it provided a special unit of 100 beds (later increased to 300) for cases of encephalitis lethargica; in 1928 it established a clinic for treating cancer of the uterus by radium. At White Oak Hospital, Swanley, chronic cases of eye disease, especially trachoma, were treated. This work helped to eradicate trachoma from the Poor Law schools.

The Board also associated pathology and bacteriology with its hospital services. In 1904 a laboratory was opened at Belmont, in 1913 a research pathologist was appointed, and two large new laboratories were opened in 1927 to conduct research work.

In 1909 Queen Mary's Hospital for Children was opened at Carshalton, Surrey, under the able direction of Dr. Pugh. Orthopaedic cases were treated here, and in 1926 a unit for children suffering from rheumatism and heart disease was added. After 1911 the Board provided a large number of beds for the treatment of tuberculosis in London.

By the Local Government Act of 1929 the London County Council took over from the Metropolitan Asylums Board eighteen hospitals for infectious disease, nine hospitals for tuberculosis, five children's institutions, laboratories, and land and river ambulance services. These hospitals were well organized, planned, and equipped. They had prevented infection from spreading among the community, and had treated infectious disease and reduced its mortality. The Board's work and its enlightened attitude towards medical progress are deserving of the highest praise.

Hospital Services

The earliest hospitals were provided by the ecclesiastical authorities. At the dissolution of the monasteries these were abolished, and the famous hospitals of St. Bartholomew and St. Thomas survived only with difficulty. In the eighteenth century many of the other great London hospitals were built. Hospital services grew in a manner characteristic of our nation, first, largely as charitable institutions under voluntary management; afterwards, continued in the same way, but followed by official provision of hospitals on a larger scale, the two systems working side by side. Thus by 1938 a large county area would contain general and special hospitals of various sizes and purposes: general, county, and cottage hospitals, municipal hospitals provided by the county council or county borough councils, Poor Law infirmaries, maternity hospitals, isolation hospitals for infectious diseases, hospitals and sanatoria for tuberculosis, hospitals and asylums for mental disease, lying-in institutions, hospitals or homes for women and children, and hospitals for special diseases—venereal, skin, eye, ear and throat, orthopaedic, etc.

The Local Government Act of 1929 greatly increased the hospital resources of county and county borough councils and gave opportunity for co-operation between municipal and voluntary hospitals. Certain authorities, notably the London County Council, made full use of their powers under the Act with the ready support of the voluntary hospitals and the local medical profession; others remained backward in this respect, and many rural areas were without adequate hospital provision and full facilities for modern medical treatment and diagnosis.

Industrial Hygiene

The study of industrial hygiene in England was initiated by Aikin, Percival, Ferriar, and Thackrah. Out of it came Lord Shaftesbury's humane Factory Acts. Dr. E. H Greenhow made investigations into occupational diseases for the General Board of Health and the Medical Department of the Privy Council, and medical inspectors of the Local Government Board reported on anthrax.

The Factory Department of the Home Office had its origin in the appointment of four inspectors of factories after the passing of the Factory Act of 1933. It was not until the appointment of Sir Arthur Whitelegge as Chief Inspector of Factories in 1896 that rapid advances were made in safeguarding the health of the industrial worker Whitelegge's appointment was administrative and non-medical, but he speedily applied his public health experience to the problems of industrial disease. Following on a Royal Commission, the Factory Act of 1878 had been passed. The amending and consolidating Act of 1901 applied to all factories and workshops, provided generally for their sanitation and ventilation, for safety, for reporting and investigating of accidents and industrial diseases, for the regulation of hours, holidays, overtime, and nightwork, and for the fitness of young persons for employment. It made special provisions for certain dangerous and unhealthy processes, while other processes of this nature were left to be dealt with after due inquiry by the Home Office.

In 1898 Dr. T. M. Legge, afterwards Sir Thomas Legge, was appointed the first Medical Inspector of Factories. He was responsible for much pioneer investigation of occupational risks in health and for legislative measures for their prevention. He studied the effects of toxic substances used in industry, such as lead, arsenic, and phosphorus: and it is mainly due to his work that persons employed in handling these substances can do so with safety. In 1896 lead-poisoning became notifiable. In 1900, 1,058 cases were notified, whereas in 1945 there were only 46. Legge's work also practically abolished the risk of cataract among glass-workers.

Other triumphs of industrial medicine have been the diminished incidence and mortality of anthrax, the prevention of mule-spinners' cancer, and the prevention of trinitrotoluene poisoning in munition factories during the war of 1914–18. Industrial hazards of various types, such as silicosis, asbestosis, occupational cancer, the toxicity of organic solvents, industrial dermatitis, and numerous other conditions, have been investigated by medical officers of the Department, and their recommendations, when necessary, have been strengthened by

legislation. The research work of the Industrial Health Research Board (Medical Research Council) and of the Industrial Pulmonary Diseases Committee of the Medical Research Council has thrown much light on many industrial problems—for instance, the pneumoconiosis of coal-miners and the byssinosis of cotton operatives. The Factory Act of 1936 consolidated previous Factory Acts.

During the second world war the Factory Department of the Home Office was transferred to the Ministry of Labour and National Service. The health of the industrial worker was safeguarded by the Factories (Medical and Welfare Services) Order of the Ministry of Labour and National Service, by the application of the results of medical research to his protection, and by the appointment of medical officers and nurses in armament and munition factories. There is still need for the more comprehensive development of industrial health services.

Mental Care

In the nineteenth century it began to be appreciated that arrangements for the care of the insane were unsatisfactory. Parliamentary Committees made many inquiries, and eventually the Lunacy Act of 1890 was passed. This made county councils and county boroughs the authorities for maintaining asylums and providing accommodation for all persons of unsound mind who could not be maintained elsewhere.

In 1924 a Royal Commission was appointed to examine the state of the law relating to lunacy and mental disorder, and reported in 1926. Thereafter came the Mental Treatment Act, 1930. This Act, in addition to including the provisions of the Lunacy Act, 1890, devolving responsibility for the care of the necessitous insane on counties and county boroughs, provided that the councils must appoint a special committee for the purpose. These councils might be combined in joint committees. The Act further provided for voluntary treatment for mental illness in public mental hospitals and that temporary treatment might be given without certification. It expunged the words "asylum" and "lunatic" from official nomenclature, except in relation to "criminal lunatics," etc.

The Mental Deficiency Act, 1913, conferred further powers on the county authorities in regard to mentally afflicted persons who were not certifiable as lunatics. The authorities had to set up mental deficiency committees. Local education authorities were made responsible for the care of mentally defective educable children at a special school, or otherwise.

The main supervision of the administration and institutions of local authorities dealing with mental disease and mental deficiency was vested in the Board of Control, which was under the Minister of Health. The Minister of Education is concerned with the care of educable mental defectives of school age, while the Lord Chancellor's functions are judicial and chiefly relate to the property of persons of unsound mind.

The National Health Services Acts

The trend of modern policy and legislation up to 1939 was to place the control of medical services and hospitals in the hands of the larger authorities—the county councils and the county borough councils. The nuclei of a comprehensive medical service were already present in the Insurance Medical Service, the Public Assistance Medical Service (formerly Poor Law), the health services and hospitals of the local authorities, and the specialist provision made by municipal and voluntary agencies.

Although excellent results had been secured, the machinery of public health organization was unwieldy and cumbersome. A number of small local authorities had inadequate resources for their public health duties; various health services were not planned comprehensively but were established independently to serve some special need. The last piece of *ad hoc* legislation was the Cancer Act, 1939, which was passed to provide increased facilities for the diagnosis and treatment of cancer.

The war of 1939–45 further emphasized the need for reform of the public health service. The Emergency Hospital Service integrated and improved the work of voluntary and municipal hospitals. The Emergency Public Health Laboratory Service established by the Medical Research Council in collaboration with the Ministry of Health became an integral part of the public health service of Great Britain, and the Hospital Laboratory Service set up by the Emergency Medical Service promoted and extended pathological facilities to hospitals throughout the country. A Blood Transfusion Service saved many lives.

Even in the midst of waging a struggle for national existence the British Government found time to pay attention to education, health, and social reconstruction. An Education Act was passed and White Papers were issued on a National Health Service and a system of universal compulsory State insurance, based on the Beveridge Report of 1942.

In 1946 and 1947 the National Health Service Acts were passed by which the Minister of Health and the Secretary of State for Scotland are to promote a comprehensive health service for the improvement of the physical and mental health of the people of England, Wales, and Scotland, and for the prevention, diagnosis, and treatment of illness. The Acts came into force on July 5, 1948.

The Acts unify the health services, but the major local authorities have a less important part in their administrative control than heretofore. They remain responsible for local health clinics and domiciliary services, but for hospital and specialist services, blood transfusion, and bacteriological laboratories the Minister assumes direct responsibility and entrusts the actual administration of the hospital and specialist services to new regional and local bodies established under the Acts. General practitioner and dental services are under the control of the Minister.

Other important recent Acts are the National Insurance Act, 1946; the National Insurance (Industrial Injuries) Act, 1946, which establishes compulsory insurance for accidents for everyone in insurable employment; and the National Assistance Act, 1948, which provides a comprehensive system of welfare and marks the "final break up" of the Poor Law.

Conclusion

The complete story of legislation in relation to Medicine during the past fifty years would require several volumes. It has been possible here to review only the principal Acts of Parliament relating to public health passed during this period of time, and to indicate their influence upon the health of the public from the standpoint of reasonable assumption. There are many things omitted—for example, the important Therapeutic Substances Act, legislation in relation to seaports and airports, and the wide subject of international health legislation. But the subjects dealt with here should give the reader some idea of the revolutionary changes which have occurred in Medicine since the present century began and of the benefits conferred by medical progress and research which have been translated into law for the common weal.

FIFTY YEARS OF PROGRESS AS SHOWN BY VITAL STATISTICS

BY

PERCY STOCKS, C.M.G., M.D., F.R.C.P.

Chief Medical Statistician, General Register Office

The Registrar-General's Annual Report for 1898 tells us that in a population of about 31½ millions in England and Wales there occurred 552,141 deaths, of which 86,755 were attributed to "zymotic" diseases. Fifty years later, in 1948, the population had increased by 12 millions but the number of deaths was actually smaller by 82,243, giving a crude death rate of 10.8 per 1,000 compared with 17.6. The group of diseases called "zymotic" in 1898 produced only 7,490 deaths in 1948, and their contribution to the total death rate fell from 2.76 per 1,000 living to 0.17, or one-sixteenth of its value 50 years before. From all other causes the total deaths were almost the same in the two years despite the great increase in population.

Indices of Progress

Crude death rates have ceased to be reliable indices of the improvement in healthiness of the people since the first world war, the reason being that the cumulative effect of falling births and declining death rates among young people began to produce a rapid rise in the proportion of elderly people in the population. In 1901 the number of persons aged 65 and over in each thousand was 47, and in 1921 it was 60, but by 1947 it had increased to 105; and since the old necessarily die at a much greater rate than the young this has had the effect of keeping the crude death rate at all ages almost constant at about 12.2 notwithstanding a progressive fall in death rates at every age.

The comparative mortality index, which corrects for changes in the population structure and expresses mortality in terms of that in 1938 as unit, gives the best general indication by a single figure of the effects of hygienic and therapeutic advances in keeping people alive longer. These indices are shown in Table I, together with the infant mortality rate and death rates at ages 5–10 and 55–65.

TABLE I.—*Indices of Mortality from All Causes in England and Wales, 1896–1900, 1921–30, 1938, and 1948*

		1896–1900	1921–30	1938	1948	1948 as Percentage of 1896–1900
Comparative mortality at all ages	M	1·825	1·163	1·000	0·815	45
	F	1·951	1·224	1·000	0·789	40
Infant mortality per 1,000 live births		156	72	53	34	22
Death rate at ages 5–10 per 1,000		4·12	2·42	1·87	0·75	18
Death rate at 55–65 per 1,000	M	34·1	24·6	23·1	21·6	63
	F	27·4	18·3	15·5	12·2	45

The death rates of infants and of children aged 5–10 are about one-fifth of what they were half a century ago. Out of 100,000 females of all ages living in 1938, 1,083 died in the year, and after allowing for changes in age distribution of the population the corresponding number in 1948 was 855. This is comparable to an annual average of 2,114 at the mortality rates current in the period 1896–1900. That is what is implied by saying that their comparative mortality index is now only 40% of what it then was. In other words, to every two females now dying in a year there would have been added three more half a century ago, supposing the populations to have been of the same size and of the same age distribution. For males the improvement has not been quite so great: to every nine males now dying in a year 11 more would have been added.

Death Rates by Sex and Age

The ratio of male to female mortality at all ages, adjusted to allow for the differences between the age distributions of the male and female populations, has tended to rise throughout the past century. In 1846–50 it was 1.088, indicating an average male excess, age for age, of 9%; in 1896–1900 it was 1.178, the excess having increased to 18%. By 1931–5 it was 1.276, and in 1947 it was 1.389, representing a male excess of 39%. The ratios of male to female death rate at successive age groups in 1896–1900 and 1948 are shown in Table II.

TABLE II.—*Ratio of Male to Female Death Rate and Relative Decrease in Mortality of Each Sex*

Age Group	Ratio of Male to Female Death Rate		Decrease in Death Rate (% of Initial Rate) from 1896–1900 to 1948	
	1896–1900	1948	Males	Females
0–	1·18	1·28	84	86
5–	0·99	1·42	78	85
10–	0·97	1·16	72	77
15–	1·07	1·16	64	67
20–	1·18	0·99	69	62
25–	1·15	1·06	71	69
35–	1·22	1·29	72	73
45–	1·29	1·55	55	63
55–	1·24	1·77	37	55
65–	1·17	1·53	28	45
75–	1·13	1·28	24	33
85 and over	1·09	1·15	26	29

The magnitude of the proportionate fall in death rate of females during the 50 years diminished with advancing age from about 85% for young girls to 62% at 20–25, then increased again to 73% at 35–45, after which it decreased regularly to 29% for the very old. It is often stated that the death rates of elderly people have not changed appreciably, and the further deduction is made that they are not likely to fall much in the next half-century; but neither the statement nor the deduction can be supported by the figures. It is true that during the latter half of the nineteenth century death rates of females at ages over 55 changed little, although they were falling all the time at ages before 35, and began to fall after 1875 at 35–45 and after 1895 at 45–55. From the beginning of the present century, however, the rates for each age group over 55 began to fall, and the improvement in the 50 years has been very considerable, mortality between 55 and 75 having been halved, whilst at ages over 75 it has been reduced by one-third. Appreciation of this is important, because nearly a quarter of the present female population is aged 55 and over, and the amount of increase to be anticipated in that proportion during the next 50 years depends a good deal upon the trend of their death rates.

The story has been similar for males, but with certain differences. The death rate of boys of school age fell by 75% compared with 81% for girls; and at ages between 45 and 85 the rate of improvement has been substantially less among men than among women, as shown in Table II. As a result the male death rate is now more than one and a half times the female rate for each age group between 45 and 75. This is in the main an aftermath of the first world war, removing as it did so many of the healthiest men from these groups, who in 1918 were between the ages of 15 and 45, and exposing others to hardships greater than were suffered by women of similar age. In the age group 55–65 particularly, male survival has failed to improve as quickly as that of females, with consequent increase in the mortality sex-ratio at that age from 1.24 in 1896–1900 to 1.49 in 1938 and to 1.77 in 1948. The large increase in this ratio during the period of the second world war is connected with the fact that these men were aged 21–30 in 1914. They represent the survivors of those bearing the

brunt of the first world war, who were then subjected again to exceptional stresses as civilians in the second war.

Life Expectation

Expected survival according to life tables provides another useful index of improvement, and Table III compares the position in 1945 with that 50 years before, in 1891–1900 (according to English Life Table No. 6).

TABLE III.—*Probabilities of Attaining Certain Ages and Expectations of Life According to the Mortality Rates of 1891–1900 and 1945*

	Males		Females	
	1891–1900	1945	1891–1900	1945
Survivors out of 1,000 born, expected to reach				
Age 5	750	938	782	951
15	725	927	756	942
45	577	825	619	880
65	332	599	398	725
75	159	355	211	505
Expectation of life at				
Birth	44·1	62·6	47·8	68·6
Age 1	52·2	64·9	54·5	70·4
40	25·6	31·1	27·8	35·0
60	12·9	15·4	14·1	18·1

Survival of children to their fifth birthday is now about 95 out of 100, having improved further since 1945, but at the end of the last century no more than 76 were reaching that age. According to the death rates of that period four out of ten girls and one out of three boys could expect to live to 65, assuming that the death rates remained constant, which is what a life table implies. The prospects are now very different, for seven girls and six boys out of ten being born can expect to reach 65 even if no further fall in death rates occurs. Indeed, half the girls now being born may expect to attain the age of 75.

The expectation of life expresses this in a different way as the mean duration of life to be anticipated by infants just born or by people who have just attained a particular age, on the assumption that death rates will not change. During the 50 years the expectation at birth has improved by 18½ years for boys and by 21 years for girls. Infants who survive the dangers of the first year have a longer expectation of life than those who have just been born, and in 1945 girls attaining their first birthday had an expectation of living another 70 years, the corresponding figure for boys being 65 years. These expectations were 16 and 12 years better than those of 1891–1900. At his 40th birthday a man may now expect to live another 31 years, an improvement of five and a half years; and a woman of 40 may expect to live 35 years, an increase of seven years. Even at 60 a woman's expectation of further life has improved by four years during the half-century.

Infant Mortality

The rate of mortality in the first year of life has always been regarded as a good index of progress in hygienic conditions within a community, although from some points of view the second year of life gives a better index. It is not easy, however, to obtain the death rates in the second year 50 years ago, and for many countries second-year rates are not ascertainable even at the present time. Infant mortality rates from all causes as given in official reports of a number of countries for various periods from 1901–5 up to 1948 are shown in Table IV. Some of these rates are not precisely comparable with those of England and Wales owing to exclusion of deaths of infants occurring soon after birth, but in recent years improvements in registration have eliminated many of these faults. The rates for France and those for Belgium up to 1935 are too low on this account. All rates for 1941–5 are arithmetical means of the five annual rates.

TABLE IV.—*Infant Mortality at Ages under 1 Year per 1,000 Live Births in Various Countries*

Country	1901–5	1911–15	1921–5	1931–5	1941–5	1946	1947	1948
England and Wales	138	110	76	62	50	43	41	34
Scotland	120	113	92	81	68	54	56	45
Northern Ireland	—	102	82	78	73	54	53	46
Australia	97	70	58	41	35	29	29	28
Canada	—	—	98	75	55	47	45	44
New Zealand	75	54	43	32	30	26	25	22
Belgium	148	—	100	82	87	71	64	55
France	149*	—	95	73	81	73	67	51
Italy	167	140	127	105	108	84	82	70
Netherlands	136	—	69	144	50‡	42	33	29
Sweden	85†	—	60	50	31	26	25	22
U.S.A.	—	—	74	59	41	34	32	32

* 1896–1905. † 1901–10. ‡ Average 43 in 1941–4, but 79 in 1945.

The ranking of these countries according to their infant mortality has remained remarkably constant, Italy, France, Belgium, and Canada having higher rates than England and Wales, whilst the U.S.A., Sweden, Netherlands, Australia, and New Zealand had lower rates. Scotland and Northern Ireland also had lower rates early in the century, but subsequent improvements have not kept pace with those in England and Wales. This table of progress since 1901–5 lends no support to the idea that limits can be set to further reductions of infant mortality attainable in the future. During 50 years the English rate has been halved twice over.

Stillbirths have been registered for 20 years only, but during that period the combined stillbirth and neonatal death rate per 1,000 total births has fallen from 70 in 1928 to 42 in 1948, or by 40%. In the same period infant mortality at ages 1–12 months fell from 34 to 14, or by 59%. It is no longer true, therefore, that the decline in infant wastage round about birth is lagging very much behind the improvement in later infancy.

Causes of Death

The zymotic diseases, to which 86,755 deaths were attributed in 1898, are shown in Table V, with the corresponding numbers of deaths in 1948 as nearly as changes in nomenclature permit such comparison. The causes are arranged

TABLE V.—*Deaths from "Zymotic" Diseases in 1898, with Corresponding Numbers in 1948*

Cause of Death as Described in 1898	Number of Deaths		Death Rates per Million	
	1898	1948	1898	1948
Miasmatic:				
Measles and rubella	13,260	329	422	8
Influenza	10,405	1,240	331	29
Whooping-cough	10,175	748	324	17
Diphtheria	7,661	156	244	4
Enteric fever	5,708	48	182	1
Scarlet fever	3,548	36	113	1
Smallpox	253	0	8	0
Chicken-pox	116	10	4	0·2
Typhus	47	0	1	0
Mumps	59	16	2	0·4
Cerebrospinal fever	11	300	0·4	7
Other miasmatic illnesses*	166	—	5	—
Diarrhoeal:				
Cholera, diarrhoea, and dysentery	30,096	3,131	959	72
Malarial	91	11	3	0·3
Zoogenous:				
Cowpox, vaccination effects	26	5	0·8	0·1
Anthrax, splenic fever	18	1	0·6	0
Hydrophobia, glanders	6	0	0·2	0
Venereal:				
Syphilis (not including G.P.I., tabes, aneurysm)	1,801	705	57	16
Gonorrhoea, stricture of urethra	335	183	11	4
Septic:				
Puerperal fever	1,707	187	54	4
Erysipelas	970	51	31	1
Pyaemia, septicaemia	251	193	8	4
Phagedaena	45	140†	1	3
Total	86,755	7,490	2,763	172

*Mainly ill-defined fevers. † Cellulitis, acute abscess.

in descending order of their frequency within each of the groups used in 1898.

The table speaks for itself. The one cause showing a noteworthy increase is cerebrospinal fever, only 11 deaths from which were recognized in 1898; but there were 7,556 deaths attributed to "inflammation of the brain and meninges" compared with about 700 in 1948, so this apparent anomaly is almost certainly to be explained by better diagnosis of the meningococcal infections. Cholera had 1,103 deaths assigned to it in 1898; but how many of this total were true cholera is doubtful, and they have been grouped with deaths from dysentery and diarrhoea of unspecified cause. For uniformity with the other causes in the table the puerperal fever rates have been based on the total population.

Amongst the reasons for the extraordinary reduction in the death rate from this group of "zymotic" diseases by 94% must have been:

(*a*) Improvements in water supplies and sanitation, virtually eliminating cholera and enteric fever and contributing to the great reduction in other diarrhoeal diseases.

(*b*) Decline in virulence or increase in natural immunity—e.g., scarlet fever, influenza.

(*c*) Protection of the community by public health measures against infection—e.g., diphtheria, smallpox, typhus, anthrax, malaria, hydrophobia.

(*d*) Improvements in personal hygiene, education, housing, and medical care resulting in reduced fatality—e.g., measles, whooping-cough, diphtheria.

(*e*) New discoveries in chemotherapy, reducing fatality from streptococcal diseases, puerperal fever, venereal diseases, and complications of measles and whooping-cough.

The respective contributions of these to the total improvement for this group of causes of death cannot be estimated except where powerful measures were introduced rapidly and on a large scale, as in the case of the sulphonamides and penicillin, which began to affect death rates appreciably in 1937 and 1945 respectively. In Table VI the trend of

TABLE VI.—*Crude Death Rates Per Million Females from Causes Mainly Due to Streptococcus and Pneumococcus. Puerperal Sepsis Rate. 1928–47*

Cause Group*	1928–30	1935	1936	1939	1942	1945	1946	1947
Puerperal sepsis (excluding abortion) per 100,000 live and still births ..	154	134	118	63	42	24	18	16
Scarlet fever, erysipelas, septicaemia, cellulitis	62	58	54	27	19	17	12	10
Ear and mastoid disease	30	29	29	23	17	17	15	14
Appendicitis, peritonitis, cholecystitis	106	116	113	97	71	61	57	52
Lobar pneumonia ..	203	174	177	126	106	91	90	91
Acute bacterial endocarditis	23	26	24	23	23	14	12	11

mortality of females since 1928–30 is shown from several groups of diseases (some not included in the zymotic diseases) for which those drugs have been beneficial.

Mortality from the first two groups was being affected by other causes before 1937, and the downward trend was then greatly accelerated. For the next three groups mortality was not changing consistently (the high rate for lobar pneumonia in 1928–30 being due to the very exceptional year 1929), but it began to fall after 1936. Bacterial endocarditis showed no fall until the advent of penicillin.

In 1898 the deaths assigned to tuberculosis (including "tabes mesenterica") totalled 60,139, and in 1948 tuberculosis deaths were 21,983. The comparative mortality index for the period 1896–1900 was 3.125 and in 1948 it was 0.826, indicating a reduction of 74% when allowance is made for changes in age distribution of the population and changes in classification.

Deaths from violent causes numbered 20,278 in 1898 and 18,716 in 1948. The crude death rate from accidents caused by vehicles and horses in 1898 was 84 per million, and the rate attributed to road transport in 1948 was 92 per million, a very small increase when the advent of motor road vehicles is considered. For burns and scalds the rate fell from 74 to 14 per million; and for all other forms of violence it decreased from 488 to 324 per million.

For all causes of death other than the zymotic diseases, tuberculosis, and violence the death rate was 12.3 per 1,000 in 1898 and 9.7 in 1948.

Certificates of Cause of Death as Instruments of Research

There is sometimes a tendency to decry the death certificate as an imperfect source of knowledge, and to suggest that in some Utopian future morbidity records will be available of such precision that it will be possible to consign death certificates to the rubbish heap of outworn instruments. For such an idea there is at present no vestige of probability, notwithstanding the fact that 1950 sees the emergence on the scene of the first comprehensive International Statistical Classification of Diseases, Injuries, and Causes of Death. That morbidity statistics will make greater contributions than in the past to public health and research, both national and international, is beyond question; but, if only because the average person consults his doctor some 300 times but dies only once, they are not likely to supplant mortality statistics.

The present somewhat cynical notion that causes of death after 65 are not of great importance can be only a passing phase. Lengthening of the average span of life has proceeded so rapidly that we have not yet grasped all that is implied by the expectation that half the girls now being born will live to 75 and half the boys to 70. With a readjustment of values, preservation of a life at 70 will take its rightful place as no less important than was the saving of a life at 50 half a century ago; and causes of death at advanced ages will demand more careful attention than is given to them at present.

This will be no easy task for the doctors who have to certify deaths, for a study of present certificates shows how complex the certification of causes at advanced ages is becoming. Amongst the young a single cause of death often suffices to tell the story, but in later life that is generally not true; and the conscientious certifier must endeavour to set out in logical order a combination of conditions which eventually culminated in death. Writing in 1887 on "Fifty Years of Civil Registration" in the 50th Annual Report, the Registrar-General said: "There is still also much occasion for the exhortation addressed by the Presidents of the Colleges of Physicians and of Surgeons that they should give such certificates of causes of death as might further the advance of medical science. . . ." This is still true to-day, though great credit is due to the large majority of doctors for their manifestly sincere efforts to obey that exhortation of more than a century ago.

The reason why some 14,000 inquiries for clarification or fuller information concerning certified causes need to be sent annually is partly because of the increasing detail of classification demanded by the users of medical statistics—that is to say, by the medical profession itself. Large numbers of certificates, however, are still filled in without due regard to the instructions provided, and in the text volume of the Statistical Review for 1940–5 (pages 81–83) the Registrar-General has called attention to defects in certification and how many of them could be avoided.

In the absence of mortality statistics derived from death certificates a review of 50 years' progress would of necessity have consisted of one great question mark. Given the full co-operation of the medical profession in the difficult and somewhat thankless task of writing down causes of death "to the best of my knowledge and belief," a review of progress 50 years hence will tell the story in much more illuminating fashion than has been possible to-day.

MEDICAL PROGRESS FROM 1850 TO 1900

BY

CHARLES SINGER, M.D., D.Litt., D.Sc., F.R.C.P.
Professor Emeritus in the University of London

The preceding articles survey the progress of medicine from 1900 to 1950. So that the reader may see this in perspective Professor Singer here traces the development of medical ideas in the fifty years before 1900.

History does not really accommodate itself to those exact dates and places that we learned at school. The Norman Conquest did not begin and was not ended at Hastings on October 14, 1066. The struggle extended over a far wider area, started generations before, and was not completed till long after—if it ever was completed. And so with the history of medicine. It is a deceptive anecdotal simplification to write it as though it consisted of a series of great discoveries each made by a particular investigator in a named year. Knowledge seldom advances by such precise and measured steps. Were I to follow that method here, this little essay would be a mere list of names and dates, and misleading ones at that.

It must be remembered, too, that discoverers no more work by themselves than do other men. Each is necessarily a member of a society—a community of men much like himself. Even the most austere and secluded man of science must have some audience in his mind—why else should he publish his results? He derives knowledge and ideas from his predecessors. He discusses his work with his colleagues. They criticize it. For some of his data he must depend on his co-workers and assistants and even on his opponents. Movements are greater than men; let us then follow them rather than the mere sons of Time. I have, for once, excluded all names from my narrative. The reader will doubtless supply them for himself.

The intellectual motives which lay at the root of medicine between 1850 and 1900 differed very considerably from those of the following half-century. To one who would contrast them with as little trouble and as much pleasure as he may, I would say: "Read two magnificent novels dating from the middle of the two periods, *Middlemarch* (1872), by George Eliot, and *Martin Arrowsmith* (1925), by Sinclair Lewis." A comparison of the characters and careers of the medical heroes in these two masterpieces, Lydgate and Arrowsmith, will go far to attaining the purpose of this number of the *British Medical Journal*.

In the decade around 1900, with which I must end my story, there were several highly significant redirections of medical thought. I am not now concerned with these. My task is rather to indicate how there arose the intellectual and scientific situation which determined them. It will be a generation before anyone will be able to say with assurance whether this year of 1950 and its surrounding years can also be regarded as a critical period for the history of medical science—for medicine is now indeed a science, which it was not in 1850. But to make history intelligible we must somehow divide it into periods. It is, then, truly the case that the years around 1900 provide a favourable and convenient opportunity for beginning to take stock of the state of medicine now. 1900 or a decade or two earlier is, moreover, about as far back as the scientific memory of living individuals usefully extends. On the other hand, 1850 is not a very tractable beginning, and I wish that I could have chosen another year for that purpose. In considering nineteenth-century medicine it must be remembered that the British medical schools have a peculiar history that differs fundamentally from that of the Continental schools. The British schools were later in coming into being. They arose actually, or by imitation, or by tradition, from a system of apprenticeship. The Royal Colleges in Britain, which came largely to control medical practice in the nineteenth century, were formed with the ancient Guild Companies of Craftsmen and Merchants in mind. An actual apprenticeship was once part of the normal career of a medical practitioner. The influence of the universities on medical thought and on medical education in Britain was trifling. It was also slightly artificial, except at Edinburgh. The great majority of students and a large proportion of teachers took only the examinations of the Colleges. The teachers in each school formed a close corporation. On the Continent, on the other hand, it was the medical faculties of the universities that were the effective agents of medical education. They too were the natural centres for scientific and medical research. Continental universities were under governmental control and had governmental financial support, conditions then quite unknown in this country. In nineteenth-century England the only branch of medicine that was the object of attention from the State was that known as "preventive." Towards the very end of the period tropical medicine also aroused some official interest.

Administrative Interest in Medicine

The great Public Health Act and the Nuisances Removal and Diseases Prevention Act were passed in 1848. They came to be operated by a new Government department, the General Board of Health. The work of this Board was taken over, for administrative and political reasons, by the Privy Council. The Medical Department of the Council became part of the Local Government Board (1871), the functions of which were, in the twentieth century (1919), absorbed by the new Ministry of Health.

Just as the General Board of Health came into action there was an outbreak of cholera in England, of which some 54,000 persons died. Statistics available under the new system made possible the deduction that the infection was conveyed by drinking-water. This led to suitable precautions. It is one of the many instances in which preventive practice preceded any knowledge of the organic cause of a disease, or indeed any direct knowledge of disease germs at all. Unfortunately, such successes—which were not a few—were often misinterpreted in such a way as to encourage faith in an attitude wrongly described as "practical." With this vague and foolish word ignorant men have comforted themselves for centuries. With it they have sought to conceal from themselves and from others their destitution of anything in the nature of general

ideas. They have done this from the days of Plato to our own, and their repetitive eloquence has often succeeded. Medicine in England has suffered sorely from "practical" men. Until the present century they kept in a relatively subordinate position the study of the basic sciences of pathology and bacteriology, while these studies were rapidly developing in Continental schools.

The Scientific Atmosphere

Let us turn now to consider the general scientific atmosphere about the middle of the nineteenth century. Men were then coming under the overwhelming influence of certain conceptions on the nature of our world which profoundly impressed almost every department of mental activity. Of these ideas the first in importance, though not in time, was the doctrine of energy, its conservation, its indestructibility, and its transformability. This view began to emerge clearly in the 'forties, and by about 1865 had taken full possession of the scientific field. Above all the velocity of light, determined in 1849, was shown in 1867 to be identical with that of electromagnetic waves. Some decades earlier the atomic view of matter had become generally accepted and had been linked with the molecular theory. By 1870 the discovery of periodicity in the properties of the chemical elements held out hope for a completer synthesis of the physical sciences. The idea of the transmutation of forces was by then a commonplace. Thus by the middle of our period there had fully developed the classical "billiard ball" view of the material world. This, it was held, consisted of untold numbers of spherical, impenetrable, inelastic, indestructible atoms. They were arranged in molecular groups in an all-pervading medium of "ether." The weightless, perfectly elastic ether in some mysterious way transmitted, transmuted, or stored forces which acted on the atoms. The older medical men who are now living were reared in that conception. It prevailed until almost the dawn of the twentieth century and induced the "positive" attitude that ultimate scientific truth was only just round the corner. This suited well the medical temper of the age. Its collapse corresponds closely in time to the end of our period.

To this "billiard ball" theory had to be fitted a very imperfectly formulated conception of the nature of life in general and of the life of higher animals in particular. The fit was a poor one, though the successful synthesizing of one organic compound after another repeatedly gave rise to hopes of finding a "physical basis of life." But the incompleteness of the fit was almost forgotten in the enthusiasm aroused by the attractively publicized doctrine of evolution. By the mid-'sixties the evolutionary origin of organic forms had come to occupy most biological thinking. Especially it stimulated interest in animal structure. Human anatomy thus became, as of old, healthily allied to comparative anatomy. It was more intelligently studied.

This was not entirely a gain to medical education, since anatomy now assumed an excessive share in the medical curriculum. The great physiological advances of the period were of high significance for medical practice, yet they produced no general idea comparable in arresting power to that of evolution. Moreover, anatomy was the necessary discipline for surgery. Vast improvements in surgical technique came with the dramatic introduction of anaesthetics from about 1850 and of antiseptics from about 1870. Anatomical detail thus gained a prestige out of all proportion to its application in general practice. The brilliance of the surgical revolution blinded men to the statistical evidence that far more lives could be saved by preventive measures than by even ideal surgery. In most English schools, too, anatomy was taught by surgeons—normally a prosperous class. If the reader adds to these things that the stipends of the teachers of preclinical subjects were paid from students' fees, that medical and surgical teachers were unpaid and depended for their livelihood on patients sent to them by past students, and that the teachers were effectively a self-electing body, he will find a diagnosis of the defects of English medical education between 1850 and 1900 no very difficult task. It was a bad system, and it is well that it has gone. Like all systems, good and bad, it produced some excellent men.

Developments in Knowledge of Function

During the second half of the nineteenth century certain fundamental generalizations on function were giving hope of a much more synthetic view of the workings of the body than any yet conceived. The hope was disappointed, but I would select as specially significant a few of the lines of development that were then current.

First was the cellular view of life and the allied doctrine of protoplasm. From these emerged two important results. One was cellular pathology. This has remained as a useful theoretical and practical foundation for the study of diseases. The other was a knowledge of what was then a wholly incomprehensible series of nuclear phenomena. This was to determine the whole conception of heredity, and indeed of life itself, in the next century. It is often forgotten how well known were the phenomena of nuclear mitosis long before meaning could be attached to them.

Second was the study of metabolism and nutrition. Important opening events here were the demonstrations, in the decade 1848–58, of the glycogenic functions of the liver and of the action of the pancreas. The 'sixties and 'seventies revealed many enzymes and their actions, involving an unexpected complexity of the digestive processes. In 1880 a new type of pancreatic and later of gastric fistula provided convenient means for a much wider range of research, leading to the conception of "conditioned reflexes." It was not till the twentieth century that the study of nutrition assumed its national and international significance.

Third was the progressive demonstration of the primacy of the nervous system, leading to the doctrine of the neurone. It stamped upon medicine the conception of an immensely complex series of systems for the transport of nervous impulses which determine the activities, the reactions, the whole life of the organism. This new knowledge of the nervous system entirely changed the direction of thought in many departments of medicine. The integration of the nervous system barely came within the nineteenth-century purview.

Fourth was the attainment, very late in the century, of some understanding of a relation of mind and body based on the study of conditioned reflexes. Parallel with this, and also from it, grew systems of psychology, physiological and other, which have since steadily increased in practical medical importance.

Fifth was a movement, with roots far back in time, which sought to apply purely chemical criteria to all forms of vital activity. It was near to what we now call biochemistry. In the last twenty-five years of the century the great exponents of chemotherapy were in Germany, where there were chairs of medical chemistry from the 'seventies.

Clinical Advances

The second half of the nineteenth century was rich in inventions of physical and chemical devices to aid the clinician. Some of these were hardly improved till the twentieth. General anaesthesia by chloroform, ether, and nitrous oxide gas was introduced shortly before 1850. The

methods of administration did not substantially change in the ensuing fifty years. Soon after the introduction of these drugs attempts were made to secure a painless state without unconsciousness. They were not successful until cocaine was adopted for the purpose in the middle 'eighties. Neither this drug nor its mode of application was much improved, except by injection into nerves, until the end of our period. Of anaesthetics as a great specialty the nineteenth century knew nothing. Of drugs of chemical origin of the period there are still in use such forms as chloral, the bromides and iodides, sulphonal, paraldehyde, and many others. To these must be added many antiseptics, chiefly those related to carbolic acid, and, above all, many alkaloids and other active principles of drugs of vegetable origin. The medical application of *x* rays comes almost outside the period here treated. It is one of the series of landmarks that divides the two centuries.

Of all medical advances of that time perhaps the most lasting will prove to be the revolution in the status and mode of recruitment of nurses. This began with the Crimean War in 1854. I hesitate to discuss it here, for it demands far more attention than I can give it. But somewhat parallel to the nursing revolution, and perhaps partly conditioning it, was the rise of specialization. It hardly existed in 1850, except in the sense that the departments of medicine and surgery, and to some extent of obstetrics, had long been rather artificially separated. Such further specialization as existed was mostly hardly more than quackery. True professional specialization was largely of Viennese origin. It came to England rather late, but became necessary with the diffusion of instruments that were difficult to use, as the ophthalmoscope (invented 1851) and the laryngoscope (invented 1855). The development of aseptic surgical technique in the 'seventies and 'eighties made possible a much wider range of operative procedures, which soon gathered their special exponents. Medical specialization, except for dermatology and to a minor degree paediatrics, hardly appeared in Britain till the twentieth century. Dentistry, like nursing, is of such universal importance for human welfare that it demands separate treatment.

The Outstanding Triumphs

The outstanding medical triumphs of the second half of the nineteenth century centre round the establishment of the doctrine of the germ origin of disease. It might be thought that here, if anywhere, specific discoveries must be ascribed to specific persons, yet it is really not so. The more the historian investigates the actual sequence of events the less inclined will he be to attach men's names to specific discoveries or to distort the picture of a great and continuous stream of thought by misrepresenting it as a series of steps—a Jacob's ladder leading to Heaven. In so small a compass as ours, we are employed better in indicating movements than names.

In fact long before 1850 it had been shown that certain diseases are associated with micro-organisms. Some even then believed them to be the causative factors. For generations many had strenuously denied that micro-organisms are ever spontaneously generated. But in 1859, as a culmination of centuries of experimentation, it was proved, as well as a universal negative can be, that the organisms of putrefaction and fermentation never arise *de novo*, but always from those of a kind like themselves. In 1863 the formation of highly resistant spores of the organisms of butyric fermentation was demonstrated, and somewhat similar spores in organisms of silkworm disease in 1869. Shrewd guesses regarding the essential nature of all infections were by then rife in scientific conversation. The real advance of the age was, as usual, less in ideas and suggestions than in techniques and demonstrations.

Much essential work at this time was concentrated on anthrax. Its bacillus had been seen as early as 1850. During the next decade or so it had been shown that the violence of an attack of this disease was in proportion to the number of organisms present. In 1871 the organism was proved to have a causative relation to the disease; anthrax bacilli were filtered off from infected juices, and the disease was found not to be produced by the filtered juices (which were nevertheless toxic) but only by the remaining bacilli. The organisms were obtained in pure culture in 1875. Highly resistant spores were demonstrated in them in 1876. The existence of these remarkably permanent minute bodies provided an explanation of many puzzling phenomena in the recurrence of this and other infectious diseases. By 1888 it was generally realized that the poisonous substances produced by the action of some organisms were specific for those forms. For these substances the word "toxin" had been introduced (1886). All this work was contemporary with the rise of the new surgical technique.

With knowledge of the life history and pathogenicity of the anthrax organism as model, investigators turned eagerly and successfully to other diseases. The pathogenic relations of the causative organisms of leprosy were revealed in 1874, of many organisms of wound infection in 1877 and the following years, of gonorrhoea in 1879. In 1882 came the great demonstration of the bacillus of tuberculosis, itself the brilliant culmination of a long series of investigations by many workers in different departments and notably in the microchemistry of dyes.

Infection and Immunity

The study of the infectious diseases now entered a new phase. The enemy was in clear view and was known for what he was. Solid media were fully available, and pure cultures were therefore much more easily obtainable than formerly. The introduction and improvement of aniline dyes as stains made the organisms more readily observable. Bacteriology thus arose as an independent science: it had its own exponents, far more numerous in Germany than in Britain. The twentieth century had dawned before bacteriologists were recognized in every English medical school.

An organism was satisfactorily demonstrated as having a causative relation to typhoid in 1880–1. Tetanus, cholera, and diphtheria followed in 1883, glanders in 1885, cerebrospinal and undulant fevers in 1887, the plague in 1894, and so on. Many organisms of disease were transmitted to animals, recovered from them, and transmitted again, producing the same disease with each inoculation, thus removing any chance of error about their causative relation. The last twenty years of the nineteenth century produced many bacteriological results in the laboratory that were destined to be extensively developed and widely applied during the subsequent period. Notably there then arose the scientific study of immunity.

"Active" immunity had been known for centuries. The conception became quite familiar with the introduction of variolation at the beginning of the eighteenth century and of vaccination at the beginning of the nineteenth. The word "immunity" passed into general use about 1880, when there was much discussion of the specific infectious fevers, their incubation periods, their statistical incidence, their mode of spread, their probable microbic origin, and the subsequent "immunity" conferred by their attacks. Methods of obtaining attenuated viruses for chicken cholera and anthrax, and their use as preventive vaccines, were

attained in France at this time. A triumph of active immunization was the preventive vaccination against typhoid fever introduced tentatively in France in 1888. Later it became more practicable, and was applied extensively to the army in India (1898–1900). No less important was the discovery of the agglutination of typhoid bacteria by the serum of infected patients in 1896 and its immediate application to the diagnosis of the disease.

During the last fifteen years of the century, and beyond, a preponderance in this type of work passed to Germany. This is a striking historic phenomenon related to certain social factors which we cannot here discuss. The years 1890 to 1894 were critical. New methods were being devised for attenuating toxins. It was demonstrated in 1890 that the blood serum of animals immunized against attenuated diphtheria and tetanus toxins can be used for preventive inoculation against these diseases in other animals—in other words, these animals were not only producing "antitoxins" but were also producing something which itself excited the production of antitoxins. In 1894 this method, as applied to diphtheria, was used on a major scale on human beings and was very successful. It was soon widely adopted. The induction of such "passive" immunity in diphtheria and in other diseases is now very familiar. There was from the first, and there still is, much discussion on the biochemical nature of the processes involved.

Tropical Diseases

Investigation of the so-called "tropical diseases" has always occupied a somewhat special place in medical thought. Owing to colonial commitments it was naturally a peculiarly British interest. We now recognize that some of the most important of these diseases are due to organisms other than bacteria. Some fungal and helminthic parasites of relatively little pathogenic importance for men had been known long before 1850. More important are the protozoal parasites.

The first protozoal disease to yield its secret was relapsing fever. The condition had been known in Europe since the eighteenth century. In 1847–8 and 1868–73 there had been outbreaks in London. The disease is world-wide. Its spirochaete was described in 1873. In 1879 the disease was reproduced by direct inoculation of infected blood. The insect vectors were not proved until 1904, though they had been suggested as early as 1857. Similarly, the spirochaete of syphilis was not adequately known till the twentieth century, though it had probably been figured in 1836 and the disease transmitted to apes in 1878.

For organisms so accessible and so easily seen, the history of the knowledge of the causative organism of amoebic dysentery is more intricate than might be thought. The reason for this is twofold. First, the species of parasitic amoebae were not adequately distinguished, for only certain of them produce the disease. Secondly, only certain cases of "dysentery" are due to amoebae. There are accounts of amoebae in human intestines from 1860 onward. These parasites were also found in liver abscesses. In 1889 the pathogenic forms were differentiated from the others and found in sections of ulcers and in stools. They were used to reproduce the disease experimentally. In 1899 cysts of the amoebae were described, and it was shown that these too could be used for infecting animals. The clearer definition of the amoebic disease naturally led to the more accurate distinction of bacterial dysentery, the organisms of which were isolated and cultivated in 1897.

Several naturalists in the 'sixties and 'seventies devoted themselves to the study of parasitic worms. They showed that certain of these, Filaria in particular, change their host during their life history. In 1878 *Filaria bancrofti* was seen to go through part of its development in an Anopheles mosquito and was traced into the blood of man. This was the first direct conviction of an insect as a disease carrier. Soon afterwards the malaria parasite was seen in human blood (1880) and its significance was grasped. Much research was now done on the malarial organism in human blood to elucidate the parasite's life-cycle there. Its general character was clear by 1897, when other stages of the life history of the parasite were located in the stomach wall of Anopheles mosquitoes which had fed on the blood of malarial patients. Within a few months the spores of the parasites were shown to be concentrated in the salivary glands of the insect. The secret of malaria was out.

At the end of the nineteenth century much scientific attention was being concentrated on the protozoal organisms known as "trypanosomes." A species had been seen in the frog in 1843, and between 1880 and 1890 several species had been reported in a large number of mammals in different parts of the world. In 1901 trypanosomes were first found in man associated with sleeping sickness. Similarly the protozoan Babesia was found in ungulates from 1888 onward. In 1895 it was found in cases of Texas fever and was proved to be transmitted by a tick, the first disease after filariasis to be demonstrably charged to an arthropod carrier. Malaria, as will be seen above, was chronologically the third.

Demographically one of the most formidable parasites is the hookworm, Ankylostoma. This creature is now known as the cause of "tropical chlorosis," "miners' anaemia," and conditions under various other names. That it was pathogenic had been known since 1866. In 1898 it was shown that it can penetrate the skin and reach its final home, the intestine, by devious routes. The interest aroused by this led to the investigation of numerous worms parasitic in animals and men. Many have been shown to have extremely complex life histories, involving several hosts. Parasitology became an independent science in the twentieth century.

Some Foreshadowings

In ending, we should refer to two other small adumbrations of great things that were to come. In 1892 there was a plague of field mice in Thessaly. It was eradicated by means of the *Bacillus typhi murium*, the first example of the deliberate use of a disease against a pest. In the same year it was shown that the mosaic disease of tobacco will pass the finest filters. In 1897–8 the same was found true of foot-and-mouth disease, the beginning of the study of filterable viruses in mammals and man.

The years round 1900 were, for science, about as critical as any in its long history. It suffices to mention the theory of relativity, the quantum theory, the revelation of the atom as a structure, and the evidence for the particulate nature of inheritance (rediscovery of Mendelism). These appeared within a few months of each other. Medical thought, too, was engaged on themes which were to develop out of small beginnings. Such was chemotherapy, the theory of immunity, the application of x rays and of radiation, the development of protozoology, the integration of the nervous system, vitamins, the psychology of the unconscious, the study of filterable viruses, and so on. It is not my task to treat these, but it is well to end, as I began, by reminding the reader that they represent drastic changes in the direction of medical thought. The year 1900 marks as definite a period as can be found anywhere in the vast annals of medical history.

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FIFTY YEARS OF MEDICINE

The fifty years that have passed since January 1, 1900, have witnessed most remarkable developments in the science and practice of medicine. So close do we stand to the many events which, especially in the past twenty-five years, have succeeded each other so quickly, that it is difficult to put the whole in perspective, to see the shape of things as they are. But the attempt must be made to take stock, to look back on the past fifty years, in order the better to be able to put into some kind of framework what we call Medicine. If we can succeed in doing this we shall have a better idea of the direction in which Medicine is going. In this retrospect the *Journal* is assisted by a distinguished band of contributors at the head of whom is that doyen of the medical profession Sir Henry Dale, whose working life spans the period of this symposium and whose own contributions to medical science are important milestones in the country surveyed. In the centre of this issue is a photographic supplement which tries to tell in pictures part of the story, and gives a few dates as finger-posts. The leading articles fill in some of the gaps that are left, and four Nestors of the profession bring to life for the modern generation the manners and modes of medicine as they practised it when Queen Victoria was still on the throne.

The canvas is as crowded as Frith's painting of Derby Day, but he who gazes at the multitudinous medical events of the past fifty years will be less bewildered if he sets them firmly within the frame provided by that master medical historian Professor Charles Singer in his brief but comprehensive glance at the medicine of the second half of the nineteenth century. Those outside the profession who may be sceptical about the progress of medicine should look at the remarkable evidence of vital statistics set forth by Dr. Percy Stocks. In the period 1901–5 the infant mortality rate per 1,000 live births in England and Wales was 138; in 1948 it was 34. In the past fifty years the death rate from the "zymotic" diseases has fallen by 94% and the tuberculosis mortality by 74%. What a fall for the good! "Lengthening of the average span of life," writes Dr. Stocks, "has proceeded so rapidly that we have not yet grasped all that is implied by the expectation that half the girls now being born will live to 75 and half the boys to 70." It would be arrogant for the medical profession to claim all the credit for this great improvement in the health of the people. More spacious housing, better food, improved sanitation, cleaner water supplies, bigger wages, healthier working conditions—all these things which have been furthered by such inspired social reformers as Chadwick, aided and abetted by the great public health movement which began in 1848, have contributed to the vastly better chance of a healthy life there is to-day than there was at the turn of the century. But if we want more specific evidence of the direct effect of Medicine we have only to turn to that dreaded complication of childbirth puerperal sepsis. Dr. Stocks's figures dramatically show the change brought about by modern chemotherapy: for the period 1928–30 the puerperal sepsis rate was 154; in 1947 it had dropped to 16. Short of committing the ancient sin of "hubris" the medical profession may feel proud of its achievements.

Professor Singer thinks that the year 1900 "marks as definite a period as can be found anywhere in the vast annals of medical history." Five years before, in 1895, Roentgen discovered *x* rays, and three years later the Curies discovered radium. In 1900, Karl Landsteiner wrote his epoch-making paper on the blood groups; Mendelian genetics was being discovered once more. By 1900 most of the pathogenic bacteria had been tracked down, cultured, stained, and submitted to the test of Koch's postulates. The major advances in anaesthesia had already been made with the successful use of nitrous oxide, ether, and chloroform; and the battle for relief of pain in childbirth had been joined and partly won. Lister, the bacteriologist who was a surgeon, had obeyed John Hunter's dictum and, with an admiring glance over his shoulder at Pasteur, tried to control surgical sepsis—and succeeded. As Professor Grey Turner puts it, surgery in 1900 was a great adventure. The publication of Darwin's *Origin of Species* in 1859 gave an enormous stimulus to anatomy. This in Singer's view was not entirely a gain to medical education. Big strides had been made in physiology, but no brilliant generalization seemed to be in the air to capture the imagination of those who practised and taught medicine. Yet it was there in Claude Bernard's seminal conception of the *fixité du milieu intérieur*.

At the turn of the century surgeons must have felt that they had no more territorial demands to make. What they had already achieved is told with verve by Professor Geoffrey Jefferson. He reminds us that by 1903 Mayo Robson could look back upon thirty years' experience of 2,000 abdominal operations, and that in 1895 Jonathan Hutchinson was a powerful advocate of specialism, an advocacy still being contested in some of the London teaching hospitals at least thirty years later. Two world wars since Jonathan Hutchinson's day, and the intrusion of the surgeon into psychiatry and cardiology, have indeed added strength to the scalpel. It may therefore be hazardous to suggest that surgery has now reached the peak of its achievement and that the next fifty years will see a steadily diminishing field of

professional opportunity for the surgeon. The sulphonamides and the antibiotics are making themselves mercifully felt as alternatives to the knife and the probe. Should the miracle happen—and surely it will—and a medical remedy be found for cancer (which will increasingly afflict an ageing population), if not in another fifty years, at least within an imaginable span of time, the torch-bearers of surgery will illuminate only that narrow field offered by injury to the body. In the medical millennium there will be only one kind of surgery—traumatic surgery.

The fifty years now ended have witnessed a great resurgence of medical thought, knowledge, and techniques. In the fifty years before 1900 Singer sees four specially significant lines of development: the cellular view of life and cellular pathology; the study of metabolism and nutrition; demonstration of the primacy of the nervous system; some understanding of the relation between mind and body. At no point, perhaps, do physiology and medicine come into closer contact than in the study of metabolism and nutrition. Here medical men may indeed claim to have given to physiology as much as they have received from it. What vast strides have been made between the publication of Gowland Hopkins's paper in 1912 and the isolation of vitamin B_{12} in 1948! It is too early yet to measure exactly the practical effect of modern knowledge of nutrition in the improvement of health, especially of the young. The war of 1914–18 provided dire examples of the lack of Hopkins's accessory factors; the war of 1939–45 showed how the wise parcelling out of vitamin foods protected the health of young Britons. Almost as an afterthought of his work on vitamin B_1, R. A. Peters and his colleagues discovered during the recent war British antilewisite, which now under the short name of BAL is triumphant in the treatment of metallic poisoning.

Although in 1891 Murray described in this *Journal* his treatment of myxoedema with thyroid, only one hormone, adrenaline, had been identified by 1918—and no vitamins. How knowledge has leaped ahead in nutrition and metabolism is told by the "pictograms" on pages 4 and 5 of the photographic supplement. The facts pile up, and the virtuosity of the chemist dazzles with its brilliance the modern practitioner of medicine. Grasping — indeed, gasping — for some generalization that will gather together at least some of the facts (more knowingly called data), the modern doctor sees in Hans Selye's conception of diseases of the adaptation syndrome a forcible reminder that man must adapt or perish as ingloriously as did the reptiles, the cold-blooded lords of creation in the mesozoic period. Here is an idea that is in direct descent of Claude Bernard's *fixité du milieu intérieur*. The brilliant work of Kendall, Hench, and their colleagues on cortisone, or "compound E," is showing how attempts to restore the equilibrium of the *milieu intérieur* may make the crippled walk. Sir Henry Dale's work on histamine and the relating of this to shock and allergy is surely another facet of Claude Bernard's crystal of thought. And the observation of Fields and Woods on the action of sulphanilamide showed that bacteria, too, can as little afford to have their *milieu intérieur* disturbed as can man. In 1899 Virchow inaugurated the pathological museum to which he had given his private collection of more than 23,000 specimens. Garrison wrote that the rise of modern medicine is inseparably connected with his name. But humoralism, then thought to be overcome by Virchow and cellular pathology, is now surely back in full flood.

The third and fourth special developments between 1850 and 1900 noted by Singer are "the progressive demonstration of the primacy of the nervous system" and "some understanding of the relation of mind and body." Between 1892 and 1898 Sherrington published the results of his work on decerebrate rigidity and reciprocal innervation; *The Integrative Action of the Nervous System* was published in 1906. In 1900 Pavlov's book *The Work of the Digestive Glands* appeared, and from then he went on to his study of conditioned reflexes. In 1900 *The Interpretation of Dreams*, by Sigmund Freud, brought new and disturbing ideas on the human scene. Contemporary with these three men of genius were the two great English neurologists Hughlings Jackson and Gowers. It is not possible to follow here the trails blazed by these men and so many others, but in the practice of medicine and in the alleviation of mental suffering Freud's work has been revolutionary; the opposition shown to his work during the past fifty years is some measure of the revolution.

If as a result of Freud's work medical men may now feel more confident in the possibilities of helping the person mentally distressed, the possibility of controlling physical disorders is now far beyond the imagination of those practising in 1900. "I doubt," writes Sir Henry Dale, "whether the change in the half-century in any department has been greater or more fundamental than in this"—the development in medical therapeutics. With the discovery of insulin in 1921 Banting and Best brought a new optimism into hospital medical wards. In 1926 Minot and Murphy treated pernicious anaemia with half a pound of liver a day; now it is possible to achieve the same benefits with a few millionths of a gramme of vitamin B_{12}. The story of chemotherapy is now familiar to the whole world. Sir Henry Dale describes the joint achievement of Fleming, Florey, Chain, and their co-workers as "one of the main events in the whole history of therapeutic research and its applications." Waksman and his colleagues have opened up new lines of attack on tuberculosis with streptomycin. The introduction into practice of one after another of powerful drugs has made the controlled clinical trial imperative. Clinical experience with remedies is something, as the practising doctor painfully learns, that can

be—and should be—measured, not guessed at. The medical man now recognizes the value of collaboration with the medical statistician in finding answers to problems. This is a big change in our fifty years of progress since 1900 and a recognition that medicine has, as Sir Henry Dale says, "become largely an experimental science itself." But the experts themselves warn against too blind a trust in the laboratory and the calculating machine. The sick person is a whole of incalculable diversity, and the future teaching and practice of medicine must be built as firmly upon this fact as upon the detailed complexity of scientific knowledge.

To tell the whole tale of medicine since 1900 in one issue of the *Journal* is obviously impossible. Much has been omitted. Inevitably more attention has been paid to what has happened here in Britain than in other countries. But, with the help of many able pens, outlines have been sketched in. The forms of practice have changed—how far Sir Arthur MacNalty reminds us in his record of the principal events of fifty years of public health legislation. "Legislation in public health," he writes, "is a legal ratification of medical advance and not its initiation." If, as he interestingly suggests, legislation is a measure of Medicine, then since 1900 the measure has been full and brimming over.

PROGRESS IN PATHOLOGY

Fifty years ago the hospital pathologist—when he existed—was engaged mainly in straightforward histology, blood counts, and the identification of common pathogenic bacteria by rudimentary methods. His quarters were cramped and his equipment primitive: most of the work he did with his own hands. It is a far cry from those days to the modern department of pathology in a medical school, with its four or more divisions, expert technicians, and lavish equipment. Not everyone now possesses an electron microscope or a Svedberg ultracentrifuge, but in 1900 such apparatus was not only unknown but unimagined, as were scores of the more ordinary and less costly tools of present-day work.

The pathologist of 1900 was usually a Jack of all trades: now, in a large department, he may restrict himself to one branch of the subject. Of these there are four—not including parasitology, protozoology, mycology, or toxicology as separate entities. The study of tissue changes in disease, from being a matter mostly of examining sections from human patients, has developed chiefly by resort to the experimental method. Perhaps the most important single example of this is the laboratory production of cancer, whether by transplantation or by the application of chemical carcinogenic agents, in which the work of Kennaway in this country was so noteworthy. Just as neoplastic change can now be induced by many agents, so can degenerative and inflammatory changes, with the advantage that the process can be followed from its inception, its causes defined, and its progress related to any factor suspected of influencing it. From the first production of tar cancer in 1911 to that of hypertension by restriction of renal blood supply and of hepatic cirrhosis by dietetic deficiency in more recent times, almost all advances in knowledge have come from experiment in animals. This is not to say that the method was never used in the last century, or that morbid anatomy and histology have made no advances as a purely descriptive science: the various gliomata and the reticuloses have been defined by simple observation of human material, and histological study has played an important part not only in more refined diagnosis but in observing the effects of treatment.

At the turn of the century the knowledge on which bacteriology had to build was the identity of most of the pathogenic bacteria, with methods of staining or cultivating them, and the principles of immunization. The cause of syphilis had yet to be discovered, as had nearly all of the filterable viruses. Almost all forms of active immunization in use to-day, notably the use of diphtheria toxoid, were unknown. Antigenic analysis, by which it came to be recognized that haemolytic streptococci and pneumococci are not one but many and that the salmonellas are numerous and variable, was still a long way ahead. This more intimate study of individual species was to have far-reaching consequences in the diagnosis and the treatment of disease, and particularly in the study of epidemiology. Only a few of the principal bacterial toxins were known: it was not even to be proved until nearly midway in this fifty-year period that the haemolytic streptococcus was the cause of scarlet fever. The highly selective culture media in use to-day were unknown, and another refined diagnostic device, phage typing, was naturally unheard of, since bacteriophage itself was not to be discovered until during the war of 1914–18.

The bacteriologist had begun to play his part in preventive medicine by determining the safety of water supplies: it was long before he was to do what he now does in helping to interrupt the spread of infection by many other means in hospital wards and elsewhere. But the chief contribution of the bacteriologist in this period has been the conquest of many infections by chemotherapy. The sulphonamides and antibiotics were purely laboratory discoveries, and their action was thoroughly studied in test-tube or by animal tests before they were used in treatment. It may be remarked that since they have attained their present position the work of the diagnostic bacteriologist has become increasingly heavy.

The two other main branches of pathology have arisen from almost nothing during the past fifty years. Chemical pathology in 1900 and for some time after amounted to little more than urine testing and such oddments as the

analysis of calculi. As Sir Lionel Whitby points out in the paper appearing at p. 21, it was the application of analytical methods to the blood which first opened the vast field now covered by this subject and the discovery of vitamins and hormones which led largely to its expansion. Almost our whole knowledge of the chemical basis of disease has been gained during this period, and an entire system of new diagnostic procedures has grown up with it. At the same time biochemistry has added to knowledge in other branches of pathology—for example, in bacteriology and immunology. The fourth branch of pathology is even more of a newcomer: the present importance of haematology can be attributed largely to two causes—the introduction of sternal puncture as a diagnostic measure, and the use of transfusion, one consequence of which has been the still expanding knowledge of blood groups.

Even before many of these changes had come about it came to be recognized that training in one or more of the branches of pathology was a valuable discipline for the future clinician. The pathologist began to be regarded as a consultant whose advice was worth seeking rather than as a technician carrying out specified investigations; he has also been accepted as the teacher of a science fundamental to medicine. There has been a corresponding change in the extent of knowledge expected of the student and in the conduct of examinations designed to ascertain it. The "spotting" of museum specimens, which was dignified with the name of pathology in the last century, has in most examinations given place to something rather more searching.

The impact of these advances on clinical medicine, though they have greatly aided diagnosis and in some cases completely altered prognosis, has perhaps not been an entirely unmixed blessing. During the past twenty-odd years there has been a tendency to lean too heavily on the laboratory, to depend too much on its findings in making a diagnosis. The practice of performing a series of investigations on patients in whom there is no specific indication for any of them calls for mass-production methods in the laboratory (with similar effects on the product to those seen in industry) and entails expense out of all proportion to the benefits gained. If the historian of the future inquires why the cost of some diagnostic laboratories multiplied several times over between, say, 1925 and 1950, his answer will be not merely that the scope of their work expanded greatly but that exclusion of possibilities supplanted confirmation as their main function in diagnosis.

We announce with regret the deaths of Dr. Clifford Dobell, F.R.S., and Dr. W. H. Newton, Professor of Physiology in the University of Edinburgh. Obituary notices will appear in our next issue.

THE RELIEF OF PAIN

The abolition of pain is not the primary end of medicine, but for the patient it must seem to be so; and no previous half-century in human history has seen so many victories over this age-long enemy. The first was one of the simplest and at the same time one of the most effective—the discovery of acetylsalicylic acid by Dreser in 1899. The pharmacologists have since produced many new analgesics, both coal-tar derivatives and synthetic alkaloids, but it is doubtful if any of them combine the twin virtues of efficacy and safety as well as this drug. If a prize were to be awarded to the agent which has done most to reduce human misery since 1900 it might well go to "a couple of aspirins." The recent employment of measured stimuli, such as radiant heat, to produce pain in the laboratory has put the pharmacology of pain upon a quantitative basis and is already yielding valuable results. The discovery of the first barbiturate—barbitone—by Fischer and von Mering in 1903 made available a new range of drugs and led to the quickly acting barbiturates, which, given intravenously, have become the anaesthetics for anaesthesia. The possibility of spinal anaesthesia had been demonstrated in 1885 by Corning, of New York: it was first employed on a patient by Bier in 1899, but did not come into general use until 1904. The discovery of the anaesthetic property of cocaine likewise belongs to the last century, but the introduction of the much safer procaine—at first called "novocain"—by Einhorn in 1905 cleared the way for the wide application of local and regional anaesthesia.

Alcohol injection of the Gasserian ganglion or its branches for the relief of trigeminal neuralgia holds a high place among the merciful achievements of this century. The procedure of injecting the nerve trunks at their exits from the skull was first advocated by Pitres and Verger in 1902 and Schloesser in 1903. The idea of injecting the ganglion itself occurred to Wilfred Harris in 1909 and he successfully carried it out in 1910, approaching the foramen ovale through the sigmoid notch, and he reported seven cases thus treated in 1912. Shortly afterwards Hartel published his approach to the ganglion by the anterior route. Sciatica is another common disorder responsible for much pain and suffering, and the medical historian will chronicle as a notable contribution to the relief of pain the discovery in the fourth decade of this century by the American workers—Love, Barr, Spurling, and their colleagues of the part played by the protrusion of the intervertebral disk in the causation of sciatica. The role of the sympathetic nervous system in the conduction of pain impulses is still incompletely understood. Nevertheless the interruption of sympathetic pathways—a branch of surgery in which Leriche has been a pioneer—has already contributed much to the saving of pain, especially pain directly or indirectly of vascular origin, and has proved

of benefit in causalgia. The indications for sympathectomy in other painful disorders await clearer definition.

During the first decade of the century Henry Head and his collaborators were carrying out investigations which added greatly to knowledge of the pain pathways in the central nervous system and drew attention to the optic thalamus as the highest ganglion concerned in the awareness of pain. The discovery that the pain fibres take an isolated course suggested that otherwise intractable pain, due for example to inoperable carcinoma, might be permanently abolished by surgical division of the pain fibres in the spinal cord or even at higher levels. In 1911 the anterolateral columns of the spinal cord were divided with this object by Spiller and independently by Martin, both in the United States, and some time later in Germany by Tietze and Foerster, who had also carried out division of spinal posterior roots. In 1938 Sjöqvist introduced trigeminal tractotomy in the medulla for the relief of trigeminal neuralgia. In the same year Dogliotti divided part of the lemniscus in the midbrain in order to abolish pain in the opposite side of the body, and his technique has been elaborated by Earl Walker. It only remained to attack the optic thalamus itself, and this is now being done, but it is too early to assess the results.

Meanwhile prefrontal leucotomy or lobotomy, an operation undertaken for the relief of mental distress, was found by Freeman and Watts in 1937 to have an unexpected effect upon the patient's awareness of physical pain, and this operation and its variation, topectomy, have been used in the treatment of intractable pain, especially that due to inoperable carcinoma. Leucotomy does not abolish awareness of pain but eliminates the emotional reaction to it. The patient experiences pain but not suffering, and is relieved of both its recollection and its anticipation. The most recent surgery of the frontal lobe suggests that it is the amount rather than the site of the cortex removed which is important, and a limited topectomy or even thalamotomy may solve the problem of eliminating suffering without changing the personality for the worse. The use of prefrontal leucotomy for the relief of pain reopens the question of the role of the cerebral cortex in pain perception. Recent work on the anatomy and physiology of pain by Lewis, Wolff, Bishop, Weddell, Sinclair, McCulloch, Walker, and others, combined with clinical observations, promises to throw new light upon the nature of pain, particularly upon those distortions of its quality to which Head gave the name "protopathic," and should lead to further advances in the treatment of persistent pain of nervous origin.

Apart from the relief of pain when the cause cannot be removed, improved techniques developed during the past fifty years of diagnosis and treatment of the causal condition have contributed to the prevention and abolition of pain. Almost the whole history of *x*-ray diagnosis and the whole of radiotherapy fall within the period under consideration, which also includes the development of chemotherapy. It is surely paradoxical that the half-century which has witnessed all these triumphs of analgesia has also seen more pain inflicted by war, torture, and mass extermination than ever before in the history of mankind.

PROGRESS IN PUBLIC HEALTH

The appointment of the first medical officer of health at Liverpool in 1847 and the passing of the Public Health Act of 1848 provided the beginnings of community medicine in this country. The next fifty years, which saw rapid growth in the science of epidemiology, was occupied in the main in cleaning up the appalling conditions in industrial towns. Since the beginning of this century most of the energies of the public health service have been put into establishing the personal health services, but the National Health Service Act of 1946 seems to have brought to an end the period of development of the services concerned with the health of the individual. With general hospitals, sanatoria, isolation hospitals, maternity homes, bacteriological and pathological laboratories, and services for the diagnosis and treatment of tuberculosis, venereal disease, cancer, and orthopaedic defects now outside his orbit the medical officer of health turns once again—perhaps with relief, perhaps with regret—to community health.

The school health service was the first of the personal health services to be established by local authorities, and it came into being because of public concern about the bad physique of many potential recruits for the Army during the Boer War, when nearly one-third of the men volunteering for service were rejected. In the investigations which followed large numbers of schoolchildren were found to be suffering from physical defects, and it was apparent that in spite of the country's material progress many lives were stunted through poverty and ignorance. In 1899 Mr. Seebohm Rowntree estimated that over 15% of the working-class population of York were living in "primary poverty"—that is, below the minimum standard required for the maintenance of physical efficiency. (In 1936 the percentage had been reduced to 6.8. It would be even lower now.) The British Medical Association pressed for a medical service for school-children and was supported by many individuals, professional and lay. The ministry of Campbell-Bannerman, with a decisive Parliamentary majority and full of reforming zeal, accepted professional advice and laid the foundation of the school meals service in 1906. The school medical service, supervised by the newly created medical department of the Board of Education, was established shortly afterwards. The tuberculosis service came into being as part of the National Health Insurance scheme. Another essential service, though less publicized, was the V.D. service.

During the second world war this was given a strenuous test, which it passed with flying colours.

In any account of the growth of the public health services in this century tribute must be paid to the voluntary organizations and workers who were often the first in the field. With their help the maternity and child welfare service grew to maturity. Dr. Percy Stocks points out in his paper that the infant mortality rate has been regarded "as a good index of progress in hygienic conditions." Since 1900 the rate has fallen from 156 to 34. One reason for this fall is the reduction in the number of deaths from most of the infectious diseases. Fifty years ago the deaths from each of the common fevers were recorded in thousands; they are now numbered in hundreds or less, the overall reduction being in the region of 94%. Stocks lists some of the reasons for this remarkable change: they include environmental improvements, increase of natural immunity, public health measures against infection, better personal hygiene, and advances in medical treatment. No doubt the progressive improvement in the state of nutrition resulting from increased wages and a better understanding of the elementary rules of health also played a part. In some of these matters the influence of the midwife and the health visitor has been great.

At times during the past fifty years obvious deficiencies have appeared in the medical services in various parts of the country, and because voluntary hospitals could not find the money for development it usually fell to public health departments to fill the gaps. Thus pathological and bacteriological laboratories were set up, orthopaedic and physiotherapy services developed, and cancer diagnostic and radiotherapeutic clinics established. During the early phase of what has been one of the most valuable public health developments of recent years—the Emergency Public Health Laboratory Service—the Medical Research Council received much help from local authorities. Finally it is worth mentioning that the Civil Defence casualty services, organized in most areas by the M.O.H., proved a source of comfort to the public during the worst days of the war.

The medical profession may fairly claim a major share of the credit for the reduction in the number of deaths and the consequent increase in the expectation of life. In particular, the M.O.H. and the public health nurse are now seeing the fruits of their labours and those of their predecessors during the last hundred years. Doctors in the public health service have certainly had a struggle to maintain equality with other medical men, but in the past ten to fifteen years they have been greatly encouraged by the interest of eminent clinicians and research workers in "social medicine." Another most valuable asset to the reputation of the public health service has been the ability of the men who have held the post of Chief Medical Officer to the Local Government Board and, after 1919, at the Ministry of Health, for they have been among the acknowledged leaders of the medical profession.

PROGRESS IN PSYCHIATRY

The era of almost explosive development in psychiatry which began approximately fifty years ago was initiated by the great systematizing work of Kraepelin. Before his time there had been no clear differentiation of the endogenous and the organic psychoses, and psychiatrists were struggling almost wholly in the dark. His method was to study the biological course of the mental illness by a follow-up which extended over twenty or thirty years; and it was through his discovery of the common features in schizophrenic end-states, and through the demonstration that manic-depressive illnesses tended towards complete recovery however often they might recur, that the foundations of the present methods of psychiatric classification were laid. It is not too much to say that without this fundamental work none of the more recent advances could have been made. Kraepelin's ideas have been enlarged and redefined, particularly by Bleuler, who showed that Kraepelin's "dementia praecox" should be widened to include all the disorders now called schizophrenic. Later work made it possible to distinguish between psychotic processes and neurotic reactions, the first having a predominantly biological causation, the latter being to a large extent the product of psychological strains and stresses. Work on the inheritance of these states has disclosed specific hereditary factors in manic-depressive and schizophrenic psychoses, but no similarly specific factors in the functional disorders of personality.

It was to these functional disorders that Freud and his successors turned their main attention. Dr. John Rickman gives an account elsewhere in this issue of the way psycho-analysis has developed to affect the entire range of psychiatric thought. Before the time of Freud the idea, which is now commonplace, that the mental processes which motivate our emotions are non-rational and are largely beyond our own powers of insight was almost unknown and entirely unacceptable. This is but one of many revolutionary concepts which we owe to Freud and which have penetrated not only into psychiatry but into general thought. They have had an important influence on the literature, the drama, and the art of our time, as well as on medicine. Even now psycho-analysis is having its effect on the study of the psychology of children, the study of groups, and social psychology. If it cannot be claimed that every part of psycho-analytical theory has been scientifically proved and that none of it will ever need to be discarded, it is at least true that new insights have been given and our mode of thought has been permanently altered.

Of no less importance than psycho-analysis—to psychiatry if not to contemporary culture—has been the advent of the empirical methods of treatment of mental disturbances by physical means. Meduna's discovery of convulsive treatment, which has proved so valuable in the affective psychoses, and Sakel's insulin treatment, which is the only method known to have

some effect in shortening a schizophrenic illness—both occurred no more than fifteen years ago. Of even greater importance is the discovery of prefrontal leucotomy. How it is that lesions of the frontal lobes cause an alteration of the personality—an alteration which can be of saving value in some of the most distressing and intractable psychoses and neuroses—is scarcely beginning to be understood. The work which is going on actively in this field will help to relate the problems of psychiatry with those of neurology and the anatomy and physiology of the nervous system, and is therefore of fundamental importance. The efficacy of physical methods has been proved not only in the treatment of psychoses but also in the neuroses, where they now constitute a serious rival to techniques of psychological interpretation. Freud's discovery of abreaction and catharsis has been re-employed in a new setting, and some workers have found a theory of their mode of action based on Pavlov's conditioning experiments more useful than one developed from psycho-analytic notions. A synthesis must, of course, eventually be made: it is most unlikely that the present gulf between physical and psychodynamic theorists will persist indefinitely. The interest which has recently been shown in the so-called psychosomatic illnesses—such as the dermatoses, peptic ulceration, hyperpiesia—may perhaps provide the bridge.

No account of psychiatric advance would be complete without some mention of the special skills which psychiatry is now borrowing from other fields. The value of statistical methods in elucidating psychiatric problems is already showing itself, not least in the contributions which are made to this *Journal*. The application of psychological methods of investigation is shedding new light on those aspects of normal psychology which have hitherto been rather neglected by the psychologist but are of special interest to the psychiatrist. Knowledge is increasing about the range of variation which "normal" people may show in temperament and personality. In the next fifty years some work of consolidation and the testing of the validity of present concepts will have to be made. The well-tried methods of the statistician and the psychologist will play an important part in this necessary task.

MEDICAL GENETICS

Mendel's work was rediscovered in 1900, and the recognition that certain human traits showed Mendelian inheritance followed almost immediately. In 1902 Bateson and Saunders and Garrod not only perceived that alkaptonuria was due to a recessive factor but drew the correct conclusion about the significance of the high rate of consanguineous marriages among the parents of affected persons. The prompt verification of Mendelian laws in man reflects certain advantages which may be set against the disadvantages of the length of the generations and the absence of controlled matings: many hundreds of millions of human beings are under sufficiently close observation for anything curious or striking to have a good chance of being reported; mating is in effect largely random; and it is practicable to make a complete survey of a population. The carefully compiled pedigrees which the early Mendelians found ready to their hand have been succeeded by nation-wide surveys such as those by the Copenhagen school. Hence it is that man is the first vertebrate in which mutation rates have been measured. General genetic theory has also gained much from study of the blood groups in man. This progress has been due to their importance in blood transfusion and in the aetiology of haemolytic disease of the foetus and newborn. The genetics of the A, B, O system, of M, N, S, s, of Rhesus, and of several other systems have been established in much detail. The vast scale upon which blood-group work has been conducted has led to important contributions not only to anthropology but also in the wider field of population genetics, for far more is known about geographical variations in the frequencies of some of the human blood-group genes than about similar variations of any other genes, plant or animal.

During the last fifty years the mode of transmission of many hundreds of simply inherited, or fairly simply inherited, conditions has been elucidated. Though most of these are rare or very rare, they are of considerable importance in the aggregate and, in the case of such diseases as haemophilia or the myopathies, of great seriousness to the individual. Single major mutant genes have been shown probably to provide the genetic basis for a number of relatively important conditions, which may ultimately include diabetes mellitus in the young, thyrotoxicosis, the allergies, essential hypertension, gout, pernicious anaemia, epilepsy, schizophrenia, and manic-depressive insanity. Progress in this direction has been slow, and there is much yet to be investigated, particularly the nature of the influences that determine whether or not the possessor of the gene—the person of appropriate genetic constitution—will in fact develop the disease.

Little advance has been made in linkage studies—that is, in the mapping of the human chromosomes—apart from the sex chromosomes. Linkage relations have been established between genes situated in the non-pairing portion of the X chromosome, and J. B. S. Haldane's tentative map of the pairing portions of the X and Y remains an inspiration for the future. One or two probable linkages have been detected in the other chromosomes. Once autosomal linkages are established, however, knowledge may grow very rapidly, as has been found in other animals. The blood groups already provide marker genes for seven chromosome pairs, and it may be that real progress is imminent. If so, it can be only a matter of time before a knowledge of linkage relations will be of practical service to medicine.

Very few normal human differences are due to single major genes, and it is now realized that in man, as in many other forms, it is the polygenes which determine most normal hereditary variation and which provide the raw material upon which natural selection acts during the course of evolution. Polygenes act in systems, each gene having a relatively small effect, positive or negative, the total effect being additive and determining the heritable variability. One medically important consequence of polygenic action is the great bulk of high-grade mental deficiency—to the extent that this is based on intellectual incapacity, and that differences in intellectual capacity are inherited. To account for inherited differences in susceptibility to disease it is the polygenes that nearly always must be invoked. In spite of apparent complexity polygenic action is not particularly difficult to investigate by suitable biometrical methods, and in this field, as in others, the human species has the very great advantage of providing a plentiful supply of identical twins and thus the means for a well-controlled natural experiment.

STATISTICS IN MEDICINE

One of the characteristics of to-day's medical journals—which would certainly be not least among those which would strike the attention of the reader of half a century ago—is the increase in their statistical content and the frequent introduction of statistical methods, both elementary and highly technical. That change has not, of course, been evenly spread over the period and, indeed, is mainly a feature of the last ten or twelve years. In 1920 Lawrason Brown, the American physician, could still plead that it was important "for us to cease using the pet phrase 'my personal experience' except when we have sufficient data to support it." If we look back further, at the turn of the century Francis Galton was experimenting with methods to assist in the analysis of biological data and in problems of inheritance. In 1901 the first number of *Biometrika* was published under the editorship of Galton, Karl Pearson, W. F. R. Weldon, and C. B. Davenport. The mathematical methods developed therein by Pearson and applied by him to biology were undoubtedly slow in influencing scientific thought in general and slower still in entering the medical field. On the other hand, a long succession of students passing through "K.P.'s" hands became the agents in the spread of the ideas underlying the statistical approach. Such men as Raymond Pearl in the New World and Major Greenwood and John Brownlee in the Old began to apply the new methods to specifically medical problems. These applications were mainly limited, however, to the problems of public health and social medicine—the analysis, for instance, of infant mortality in relation to environmental conditions, the study of the epidemic curve, and so on. Clinical medicine was but little influenced, and the method of choice was still too often based upon a handful of uncontrolled cases and "my personal experience." To some extent, too, there was antagonism. The medical man charged with responsibility for the patient was contemptuous of the statistician's fundamental approach through the group; and the statistician took a jaundiced view of the conclusions light-heartedly drawn by the practitioner from a handful of cases without allowance for the play of chance.

Meanwhile the scientific field of agriculture was being quietly revolutionized by the statistical methods developed by R. A. Fisher (whose *Statistical Methods for Research Workers* was published in 1925). The introduction of these newer methods to medicine was, as before, slow, but again the general permeation of scientific thought with the statistical approach was imperceptibly making itself felt. Naturally one of the first branches of medical science to be invaded was that concerned with the biological standardization and assay of pharmaceutical products. The variability of the animals to be used had essentially to be taken into account, and the experimental design of the assay was vitally important to afford the most economical and instructive use of a given number of animals. The degree of trustworthiness of the results was clearly fundamental, and measurements of the limits of error inevitably followed. At much the same time follow-up studies of patients on a satisfactory scale began to come into vogue—of patients discharged from sanatoria or operated upon for various forms of cancer. Attempts were made to measure numerically the advantages of specific treatments such as artificial pneumothorax in pulmonary tuberculosis. Many of these studies suffered then, as now, from the handicap that no comparative observations could be made, sometimes for ethical reasons but not infrequently because their importance was not appreciated. They are far more frequently appreciated to-day, and two factors which have contributed to that result are the second world war and the rise of chemotherapy. The war led to the development of "operational research," which is in essence but another name for practical work and observation in the field, as opposed to the controlled experimentation of the laboratory. Such methods are peculiarly the province of clinical medicine. At the same time the rapid introduction of new drugs continually forced the question, Does it work? Only a statistically planned trial could show, and thus we have to-day the fully controlled therapeutic trial—whenever, it need hardly be emphasized, the moral issues can be wholly met. Similarly it is unlikely to-day that we should adopt on a wide scale the use of a prophylactic vaccine without an adequate trial of its value in the human population. Lack of such a trial early this century delayed, it may be suggested, the general use of diphtheria immunization for a generation.

Other statistical problems in which medicine has become increasingly involved lie in what might be termed the mechanization of the means of diagnosis.

The reading and interpretation of *x*-ray films, the making of blood counts, the spate of pathological procedures, these may all come to the clinician's assistance, but it should not be forgotten that they are all liable to errors. Measures of their accuracy have but recently been sought by the statistically minded. To some it may seem that the medical world has become unduly obsessed with arithmetic and the statistical approach. In retort it can be argued that the obsession may be found in too great a reliance on statistical techniques to the exclusion of logical thought, and sometimes in too great an awe of the mathematical mind. The medical statistician must be no high priest of an occult art but a partner in the solution of medical problems, to which he brings medical as well as statistical knowledge. The usefulness of this partnership can be gauged from the long list of Medical Research Council and Government committees on which Professor A. Bradford Hill, director of the department of medical statistics at the London School of Hygiene and Tropical Medicine, serves as a member. Statistical knowledge, as Raymond Pearl once wrote, is not a "higher kind of knowledge than that derived in other ways," but a valuable adjunct in most fields and an essential method in many. Even in the centenary annals of the "arch-priests"—i.e., of the Royal Statistical Society—it is stated that "mathematical analysis is an excellent machine for threshing out the facts, but the facts have first to be harvested and there is a place for even the humblest gleaner." In the next half-century we may look forward to a higher standard in medicine both of the gleaners and of the threshers.

FIFTY YEARS OF OPHTHALMOLOGY

The last fifty years may with some justification be looked upon as the adolescence of ophthalmology. At the time of the great resurgence of medicine that occurred a hundred years ago—the time of Claude Bernard, Louis Pasteur, Carl Ludwig, Virchow, Bright, and Addison—the discovery of the ophthalmoscope by Helmholtz in 1850 was so potent a stimulus that ophthalmology suddenly assumed a separate existence as the first of the great medical specialties. Its youth was one of great activity and achievement; Bowman in anatomy, Helmholtz in physiology, Donders in optics, von Graefe in clinical science, and Fuchs in pathology typified the energy and unusual brilliance of its proselytes. In the basic sciences the last fifty years have seen advances which on the whole have kept in step with those in cognate fields. At the beginning of the century the work of Leber and Wessely in Germany and of Parsons and Starling in England rationalized ocular physiology in terms of the tissue-fluid exchange understood at that time. In the late 'twenties a renewed period of activity, originating in London and Paris and later extending to Harvard and Johns Hopkins, saw the application of biochemical and, more recently, of tracer techniques to the problems of the metabolism of the eye. In fact no other organ has been so closely studied. The vast amount of information about the physiology of vision patiently collected during the previous half-century was consolidated into an integrated philosophy of perception by Parsons in 1927. During the last twenty years understanding of the mechanism of visual processes has been greatly aided by the electro-physiological researches begun by Adrian at Cambridge and continued by Hartline in America and Granit in Sweden. The subject of visual optics, which had hitherto been based on Helmholtz's work, was transformed at the beginning of the century by the researches of Gullstrand, of Uppsala, who was awarded a Nobel Prize. It was as a result of his work that simple spectacle lenses were replaced during the early days of the century by the efficient types we know to-day (Tscherning and v. Rohr). A later development, in 1933, was Dallos's work on contact lenses.

In clinical ophthalmology much has been done to consolidate and elaborate the work of the previous half-century. This is well seen in pathology, wherein the four-volume treatise by Parsons (1904–8) still remains a standard textbook. Valuable new optical techniques, however, have been worked out. Because of the transparency of its structures, which allows the observation in minute detail of the progress of pathological lesions, the delicacy of its tissues, which respond markedly to minor trauma, and the dramatic effects of its functional impairment, no organ of the body has provided better opportunities for concentrated clinical study than the eye. The greatest advances in clinical ophthalmology in the last fifty years have been the development of the slit-lamp by Gullstrand in 1911 and the able and industrious exploitation of biomicroscopy by Alfred Vogt, of Zurich, in the 'twenties and 'thirties, whereby magnifications comparable to those used by histologists can be applied to living tissues. These methods, and their extension during the last few years to include microscopic examination of the fundus, have established the existence of a great number of pathological conditions and have made ophthalmology the most exact of all branches of medicine.

In operative surgery the first half of the century has seen a steady and progressive improvement in technique, but in four of the commonest ocular diseases great changes have occurred. Before 1900 chronic glaucoma was treated indiscriminately by the ineffective classical iridectomy of von Graefe; then, in striking sequence, Herbert, in India, introduced sclerotomy (1903), Heine, of Breslau, cyclodialysis (1905), Lagrange, of Bordeaux, sclerotomy (1905), Holth, of Oslo, iridencleisis (1907), and Elliot, again in India, the trephining operation (1909). Since that time progress in the surgery of glaucoma has stopped. The second great surgical advance was the popularization of the intracapsular

extraction of cataract by Elschnig, of Prague (1909), which was followed by the standardization of the technique of corneal grafting by the same unusually gifted surgeon in the 'twenties: both of these procedures are to-day becoming routine operations. Last and by no means least was the brilliant discovery of how retinal detachments occurred and their equally brilliant cure by operation introduced by Jules Gonin, of Lausanne, in 1925. Finally ophthalmology has participated in the advances of other branches of medicine and neurology: access to the chiasmal region has been made possible by the neurosurgeons; the major role played by allergy and tissue sensitization in ocular inflammations is now appreciated, thanks largely to the work of Alan Woods, of Baltimore; and, of course, the sulphonamides and antibiotic drugs have an important place in ophthalmology as elsewhere in medicine. Taken as a whole, with its knowledge of the fundamental sciences, its unique appreciation of the intimate processes of disease, and its resources of therapeutic and operative techniques, ophthalmology may be said to have reached a virile maturity, and it should be well able to exploit any opportunities which the future may hold.

OTOLARYNGOLOGY

There have been notable achievements in otolaryngology in the past fifty years, but the specialty owes much to the discoveries and advances in general medicine and surgery. Nothing, for example, has altered diagnosis, treatment, and prognosis in otolaryngology so much as the introduction of the antibiotics: acute mastoiditis has changed its characteristics; the faces of a patient's relatives do not now blanch when the mastoid operation is mentioned; the technique of labyrinthectomy is almost forgotten; no longer does the rhinologist fear a fatal meningitis as a sequel to a simple intranasal operation. Syphilitic laryngitis is now rare, and streptomycin is changing the appearance and the prognosis of tuberculous laryngitis. The whole tone and outlook of the specialty has altered; the training is more scientific and more prolonged, the laryngologist no longer has to learn a conjurer's sleight-of-hand for intralaryngeal operations, and perhaps over-optimism has taken the place of the habitual pessimism of the otologist.

Fifty years ago the leading British otologist—Sir William Dalby, founder of the Otological Society in 1900—had never performed a mastoid operation, and laryngologists were still physicians, though some of them had begun to operate on the nasal sinuses as well as on tonsils and adenoids and the larynx. Most of the teaching hospitals still had separate departments for diseases of the ear and for diseases of the throat, but some laryngologists were beginning to take surgical fellowships. 1902 was a notable year, for Killian, of Freiburg, came over to the B.M.A. meeting at Manchester and introduced peroral endoscopy to British laryngologists. At the same meeting John Macintyre, of Glasgow, emphasized the value of *x* rays in the detection of foreign bodies; but some laryngologists protested that both Killian's tubes and Macintyre's *x* rays were unnecessary, and Walker Downie showed an imposing array of foreign bodies removed from the food and air passages by probang, coin-catcher, or tracheotomy and forceps. Killian used proximal lighting for his oesophagoscopic and bronchoscopic tubes, but in 1904 Chevalier Jackson, of Philadelphia, improved the distal lighting principle devised by Einhorn and made other useful modifications. He developed the largest clinic and school of peroral endoscopy on either side of the Atlantic, and published, in 1907, the first textbook on the subject. Almost all otolaryngologists throughout the world went to Vienna (a few to Munich or Berlin) for their postgraduate training, some for a few months, some for years, for it was well systematized there under Politzer (who retired in 1907), Chiari, Hajek, Neumann, and Haslinger. The war of 1914–18 interrupted this custom, and after the war the fame of Chevalier Jackson and subsequently of other American and Canadian otolaryngologists began to lure British postgraduates across the Atlantic, a tendency that has continued up to the present day.

In 1909 G. E. Waugh, of Great Ormond Street, published his method of complete removal of the tonsils by dissection, and in 1910 Whillis and Pybus, of Newcastle-upon-Tyne, introduced their reversed guillotine method which revolutionized tonsillectomy; Greenfield Sluder, of St. Louis, U.S.A., read a paper on a similar method in the same year, though he did not publish it until 1912. It was not until after the war of 1914–18 that the dissection method began to oust tonsillectomy with the reversed guillotine, and it was some years later still that children were admitted to hospital as a routine for the removal of tonsils and adenoids instead of being treated as out-patients.

In laryngology the results of both laryngofissure and laryngectomy for cancer of the larynx have greatly improved since the days of Butlin and Semon, not only because of earlier diagnosis and better operative technique, but owing to advances in anaesthesia and after-treatment. With these improved results the name of Sir StClair Thomson will always be associated. In recent years many cases have also been treated successfully by radium and *x* rays. In rhinology Caldwell, Luc, and Scanes Spicer had independently devised the modern radical operation on the maxillary antrum in the 1890's, but it was not until after Logan Turner (1902) had published his work on the anatomy of the frontal sinuses that Killian (1904) performed his external frontal sinus operation. Modern work on allergy has changed much of the attitude of the rhinologist to the nose and nasal sinuses. In otology Robert Bárány, of Vienna, and latterly of Uppsala (1906), Rudolph Magnus, of Utrecht (1924), and W. J. McNally, of Montreal (1925 onwards),

have added much to our knowledge of the vestibular system; the work of Wever and Bray, of Princeton (1930), has modernized without altering the theories of hearing that date back to Helmholtz; Gregg, in Australia (1941), has thrown a new light on the causation of deaf-mutism; C. S. Hallpike and Hugh Cairns (1938) changed the whole conception of the pathology of Ménière's disease; and Gunnar Holmgren, of Stockholm (1917), Maurice Sourdille, of Nantes, and subsequently of Strasbourg (1932), and Julius Lempert, of New York (1938 onwards), have developed the fenestration operation for the relief of deafness due to otosclerosis—a masterpiece of technique, even though it does not cure the disease. In the investigation of the acuity of the hearing the invention of the audiometer has been a notable development. Ear trumpets and tubes as hearing-aids for the deaf date back two or three centuries, but the first electric hearing-aid of the microtelephone type was made in America in 1898. The invention of the thermionic valve made practicable a new type of hearing-aid, and since the war of 1939–45 great advances have been made in its development.

ANAESTHETICS AND ANAESTHETISTS

The specialty of anaesthesia was born in an age of enthusiastic scientific inventiveness, and the burst of progress in the thirty years following Morton's discovery has never been repeated. Since 1900 advances in anaesthesia have been largely in the nature of consolidation of the work of its pioneers and perfection of techniques already in existence. The problems presented by surgery in this century—particularly those of thoracic surgery and neurosurgery—have been brilliantly overcome by anaesthetists, but mainly with the aid of old-established agents and the adaptation of principles exhibited by early apparatus.

The help of fresh drugs and new appliances in tackling these difficulties is nevertheless not to be belittled. Procaine was synthesized by Einhorn in 1905, and solved many problems of local analgesia. Cyclopropane, introduced by Waters in 1930, indirectly gave stimulus to the growing specialty of thoracic surgery. Trichlorethylene was established as an anaesthetic by Hewer in 1940, and has provided a safe alternative to chloroform and a new analgesic for midwifery. The first use of curare for operative surgery by Gray and Halton in 1946 allowed of a new concept in anaesthesia, though the value and limitations of this and similarly acting drugs still remain to be fully assessed. Intravenous barbiturates, which from the patient's viewpoint have been the greatest single boon since the discovery of anaesthesia itself, were first used by Weese and Scharpff in 1932. Boothby and Cotton's 1912 flowmeter, which established the important principle of measuring the amount of gas the patient received, was incorporated by Boyle in his continuous-flow machine of 1917, and in 1923 carbon dioxide absorption was used for man.

But it was before the close of the nineteenth century that Oré administered chloral hydrate intravenously, that spinal analgesia had been popularized and local analgesia attempted. The effects of crude curare on animals were ably described by Waterton in 1812. The first practical gas-and-oxygen machine, the basis of the apparatus widely used to-day, was designed by Sir Frederick Hewitt in 1892. The carbon dioxide absorption principle had been tried by the incomparable Snow in 1851, and was first used experimentally in this century by Franz Kuhn. Kuhn was the first effective practitioner of endotracheal anaesthesia (though Trendelenburg and Macewen had previously essayed the procedure), but it was left to Magill and Rowbotham, working under the vigorous stimulus of the young specialty of plastic surgery, to perfect the manœuvre shortly after the 1914–18 war and to introduce the "blind" technique. Their work has affected all branches of anaesthesia, but was never more keenly appreciated than in the plastic units of the war of 1939–45.

Outside the comparatively few special centres, the standard technique for operations to-day is based on the nitrous-oxide–ether sequence conceived by Clover in 1876; nitrous oxide and ether, the earliest anaesthetics, are still the most frequently administered; and the controversy on chloroform continues—less spiritedly but little more conclusively—as it did in 1900, the year of the Report of the B.M.A.'s Anaesthetics Committee.

Of far greater importance than the introduction of new and improved agents and apparatus is the striking advance since 1900 in the status, training, and ability of the anaesthetist. In 1896 Hewitt wrote: "Why do not deaths from anaesthetics show signs of diminution? The reply is that the responsibilities involved in administering anaesthetics are not yet fully realized; that the administration is too often placed in the hands of comparatively unskilled men. . . . The first step should be an educational one." In 1900 anaesthesia had not even a place in the medical curriculum; to-day it is recognized as a specialty equal to any other. The Diploma in Anaesthetics was initiated in 1935, and 1948 saw the establishment of the Faculty of Anaesthetists of the Royal College of Surgeons. The founding of the first British chair of anaesthesia at Oxford in 1937, through the generosity of Lord Nuffield, was a landmark of equal significance. The anaesthetist is no longer the "chloroformist" whose practice is founded on empiricism. He is the "clinical physiologist" of the operating team, who has the scientific background to use his drugs and instruments in their most effective and least harmful combination. Although the past half-century has not thrown up a Clover or a Snow, it has produced—what is more important—a marked raising of the standard of the individual anaesthetist throughout the country.

MEDICINE TO-DAY AND YESTERDAY

A RETROSPECT

BY

Sir ROBERT HUTCHISON, Bt., M.D., F.R.C.P.

I joined the staff of the London Hospital early in 1900 and am therefore in a fair position, so far as memory serves, to compare the state of medical practice—especially of course hospital and consulting practice—half a century ago with what it is to-day.

Contrasting the medical scene in the year 1900 with the present, and remembering the tendency for distance to lend enchantment, for age to be a praiser of the past, and the rosy mist through which a man is apt to view his early professional life, I still think that medicine was a more interesting, exciting, and adventurous business in the early years of this century than it is now. And that for several reasons.

In the first place, the doctor, whatever his branch of work, was much more engaged in single combat with disease and less one of a team. He went into action for the most part armed only with his own senses and a stethoscope, with a few simple urinary tests, blood films, and an old-fashioned ophthalmoscope as auxiliaries. Biochemical tests had not yet been invented (happy days !), nor were the sphygmomanometer, the electrocardiograph, and other mechanical aids to diagnosis available. Even *x* rays were only in their infancy. Still, it was more exciting to find out things for oneself and to try to come to a correct conclusion on insufficient data than simply to collate the "reports"—often conflicting—of a number of technical experts. Nor was diagnosis so bad at that time after all. It is true that its main object was to try to foretell the findings in the dead-house, but this limited object was achieved with astonishing accuracy by the physicians of those days as a result of careful history-taking, thorough physical examination, and the exercise of their "clinical intuition"—a faculty with which I think they were better endowed than their modern successors. Disorders of function they hardly aspired to determine, for functional tests were mostly still in the future.

In the second place, when one looks back disease seems to have been more varied and, if one may use the word, *florid* than it is now. The advance of preventive medicine alone has robbed the clinical field of some choice specimens. Typhoid fever—once a hardy annual in medical wards—is one. Where, too, are the "beautiful" examples of rickets and infantile scurvy, or the cases of acute rheumatism with enormous nodules which I remember so well at Great Ormond Street ? Soon diphtheria will also be a thing of the past. Surgery, too, has taken its toll. What young physician has seen an advanced case of pyloric stenosis with gastric fermentation in which the patient belched marsh gas so that sometimes when lighting his pipe the gas took fire and he seemed like a dragon breathing flame ? Yet I have witnessed this interesting and exciting occurrence two or three times before the surgeons intervened. Again, when does one now see an old-fashioned case of lobar pneumonia ending dramatically by crisis in seven or nine days ? Most cases of pneumonia in these degenerate times end not with a bang but a whimper.

Other interesting clinical specimens have vanished of themselves and for unknown reasons. Chlorosis, well named the "green sickness," for instance, of which the modern "hypochromic anaemia" is but a pale simulacrum, and, simultaneously with it, its frequent accompaniment acute gastric erosions with gastrostaxis, which latter has so bedevilled the statistics of gastric ulcer and haematemesis compiled by moderns who have never seen a case of what was once one of the commonest objects in a female ward. Gone, too, is muco-membranous colitis. the typical casts of which I could demonstrate to my clinical clerks almost any day in the early years of the century. Interstitial nephritis ("chronic Bright's," as we called it) occurring in men of middle age and often showing itself first by uraemia and proving fatal within a year is now, I understand, become a rarity.

Further, modern treatment has made it impossible to follow the natural course of many diseases. How many students to-day realize that pernicious anaemia is a disease which, left to itself, shows two or three complete remissions before finally proving fatal? Or that exophthalmic goitre is a self-limited disease ending in recovery in about three-quarters of the cases, though the patient may be left rather pop-eyed?

On the other hand, the present generation may console itself with the greater commonness of some of the old diseases and with the emergence of some that may be new. Among the former peptic ulcer, coronary occlusion, cancer of the lung, and infective hepatitis at once suggest themselves. Why they have become commoner I have not space to discuss, but I would only say quite emphatically that it is not a question of better diagnosis. Odd though it may seem, we were not altogether fools fifty years ago, and could diagnose these conditions quite well, though we may have called some of them by different names. Besides, we always had necropsies to correct our errors or oversights. As regards the appearance of new diseases in the last half-century, it is well to bear in mind the warning of Gee, that it is more likely that they have previously been "overlooked or confounded." However, encephalitis and atypical pneumonia are for practical purposes new, and of course a large number of new "syndromes" have, for good or ill, been differentiated in recent decades.

Another thing that made for greater interest in hospital work in the old days was that every physician was supposed to be a *general* physician, even though he often had a particular interest in some special branch. Patients were not segregated according to their disease, and every ward afforded a varied assortment of cases.

It is probable, of course, that disease has become less "picturesque" with each generation, and 1850 no doubt showed many more graphic types than 1900. Should medicine ever become an exact science—which Heaven forbid—it would probably be so dull that no one would want to practise it. But we are a long way from that yet.

It is in treatment, however—we never used the word "therapy"—that the present scores. Looking back, the advances are almost unbelievable. At the beginning of the century there was prevalent a good deal of therapeutic scepticism. Bacteriology, from which much had been hoped, was proving disappointing, and it was widely believed—how falsely !—that drugs were at the end of their tether. A medical ward full of advanced cases of organic disease was rather depressing ; one felt so helpless to do anything.

On the new remedies and methods which have been introduced in the last fifty years it is unnecessary to dwell in detail, but they have changed the whole picture, and as regards ability to cure, which, after all, is the main purpose of medicine, the latter days are incomparably better than the former.

It is natural for anyone with long experience of our profession to reflect on the changes in pathological theory as the years go on. In the early part of the century "auto-intoxication" and "uric acid poisoning" were all the vogue, with resulting abuse of "intestinal antiseptics" (does anyone ever prescribe them now?) and "uric acid solvents." Now it is the turn of "allergy," "avitaminosis," and "endocrine imbalance," with the consequent indiscriminate use of antihistamine preparations, vitamins, and hormones. The conception of psychosomatic medicine was not formulated in 1900, and the psychologist was a rare bird outside the asylum.

If the practice of our profession was more interesting and adventurous fifty years ago it was not less arduous. I am always inclined to be sceptical when people talk of the "strain of modern life" as explaining the increase of certain diseases—coronary occlusion, for example. As a matter of fact, the doctor of 1900 had in many ways a more exhausting life than his successor of to-day. The motor-car had hardly come in. A surgeon would dash up to the hospital in a barouche and pair, having perhaps lunched off a few sandwiches on his way from the West End; a physician would alight from a one-horse brougham, whilst the assistant staff came by foot, bus, Underground (there were as yet no "tubes"), or—on rare occasions—by hansom.

Few kept a secretary. Letters were written by hand, mostly in the evening, and eminent members of the profession could often be seen taking them out to post at midnight, for in those days letters were collected late. All this was rather wearing, especially as week-ends had hardly begun; but, on the other hand, most consultants lived "over the shop" and were spared the strain of the double life of St. John's Wood and Wimpole Street. The Cavendish Square district was then really residential, each house, even in the Square itself, containing its family and retinue of servants. It was rare to find more than one brass plate on a door. Certainly the sight, now so common, of a covey of plates, a quarter of them bearing foreign names, was then unknown. In keeping with this more dignified living there was more seemliness of dress. The silk hat and frock-coat were *de rigueur*. And a very comfortable uniform it was. I remember in the hot summer of 1911 going so attired to a consultation at Greenwich when the temperature reached a record of 100° in the shade. Nor did I feel much incommoded.

Whether consultants were better paid on the whole then than they are now it is difficult to say, especially since the muddle introduced by the N.H.S. Juniors certainly were much exploited. House-men usually got no pay at all, and registrars had to work very long hours for a mere pittance. In established consulting work the fee for a first consultation was two guineas (it was not long since it had been only one), and for a "domiciliary" consultation, within four miles of Charing Cross, three guineas. These figures went up after the first war to three and five respectively. "Country journeys," however, were probably over-paid (two-thirds of the mileage in guineas)—a relic of the days when one travelled by coach. They were also much more frequent than they are to-day, for fifty years ago there were few recognized consultants outside London except in the really large cities.

It must also be remembered that in those days there were no devalued pound notes. The sovereign was supreme and worth fully twenty shillings. Living also was extraordinarily cheap and taxation light. Take it all in all, the Edwardian era was certainly the Golden Age of consulting practice. It is improbable that anything like it will ever return.

SURGERY IN 1900

BY

G. GREY TURNER, M.S., F.R.C.S.

Emeritus Professor of Surgery, Universities of Durham and London

Surgery as I saw it fifty years ago mostly concerned the practice of the old Newcastle-upon-Tyne Royal Infirmary, a large, active provincial hospital.* In 1900 that institution had a normal complement of about 250 beds, but then and for many years overcrowding was a very serious problem. This was especially so on the surgical side, and I have seen a double row of beds all up the middle of a female ward, with one or two patients lying on mattresses on the floor, and two patients in one bed, an adult at one end and a child at the other. Receptions for each of the firms went on for a week and recurred every four weeks. By the end of that time the wards were often in an appalling state of congestion, with nurses distracted and house staff worn out.

Nature of the Admissions

The surgical wards took many more than half the admissions, and during that year 2,642 major operations were carried out. The nature of the cases was very different from what it is to-day. For instance, there were no fewer than 129 major amputations with 14 deaths, whereas only 62 cases of appendicitis were operated upon with 12 deaths, and 7 ruptured gastric ulcers with 4 deaths. Stomach surgery of the cold type was just beginning and there were only 11 such operations that year. Strangulated hernia seemed much more frequent, and among 192 hernias of all varieties there were 39 presenting that complication, with 11 deaths. Stricture of the urethra was not only a much more common condition than it is to-day, but was more serious. There were 43 cases admitted to the wards, and many of these were complicated by periurethral abscess or extravasation of urine. Every year two or three cases of tetanus were admitted, and it sometimes arose in cases operated upon in hospital. The mortality was appalling, for antitetanus serum was not yet a practical proposition.

The industrial occupations of the district were reflected in the nature of many of the admissions, and coal-miners accounted for nearly all the 34 cases of injury to the semilunar cartilages, while from the lead works on the Tyne came 36 cases of poisoning. I cannot help remarking on the frequency of thoracic aneurysm, for no fewer than 26 cases were admitted that year, and many were quite obvious externally. Alcoholic diseases were also very common, and there were 14 cases of liver cirrhosis: some cases with ascites were being treated by the omentopexy of Drummond and Morison with encouraging success.

At that time gynaecology was done by the general surgeons, and there were 53 cases of ovariotomy with 2 deaths. An *x*-ray department had just been started, but only 157 cases were examined. Genito-urinary cases had to be investigated without the help of accessory methods, for the cystoscope was still a curiosity, catheterization of the ureters was not employed, and the urine separator had not yet arrived. Bacteriology as a clinical instrument was in its earliest infancy.

A Time of Adventure

At that time practically all the operations were done in the one theatre. It is true that there was another small operating-room on the top floor of the institution, known as the "ovarian room," but it had lost its special status and was used as an occasional general theatre. It was

*The present Infirmary was not opened until 1906.

entirely without special fittings of any sort beyond a roof light, and was merely a room not ordinarily used for any other purpose. Operating tables were of wood, and to secure the Trendelenburg posture the table legs at one end were lifted up on to chairs.

Generally speaking, the work in the theatres was rather informal, and visitors gathered round the table in their ordinary clothes, as will be seen in the first picture in the photographic Supplement. Students, unless they were dressers handing instruments, were not encouraged, and if they did come in as spectators they had to stand in the tiered gallery. The theatre was frequently made a rendezvous, and was often crowded.

At that time the technique was entirely antiseptic and was conducted on strict Listerian principles, but nothing was boiled. Instruments were immersed in 1 in 20 carbolic lotion for half an hour before operation, and the towels which surrounded the operating site were soaked in Lister's strong mixture or in 1 in 20 carbolic. Fine Turkey sponges were in universal use as mops; their cleansing and care meant constant work and was always an anxiety, and was entrusted only to the most reliable nurses. Catgut was used as ligature and suture material, and various chemical methods of sterilization were tried from time to time. Almost the only anaesthetics employed were chloroform on an open mask or ether administered with Clover's inhaler. In the latter case induction was often by nitrous oxide. There were no sterilized operating garments for the surgeon, who wore linen or india-rubber aprons. It was not until two or three years later that we tentatively began to use gloves. Nevertheless, those surgeons who thoroughly understood the application of the Listerian technique achieved long runs of excellent results and for months on end wound healing would be perfect; but there was always the risk of an outburst of annoying infection, and I have seen odd cases where clean laparotomies and knee-joints became infected, the patients promptly dying from septicaemia.

It was a time of great adventure in surgery; for, having learnt how to prevent infection in operation wounds, surgeons were groping about to discover how to make the best use of the discovery.

Some Problems

The problem of the radical cure of hernia loomed large and many methods were on trial. The younger surgeons of to-day may be sceptical and perhaps even disrespectful about the Bassini operation, but I can assure them that its acceptance was an enormous advance on any of the methods employed at that time, and its general adoption was soon followed by a great improvement in the results.

There was no accepted technique for abdominal hysterectomy, which was just being laboriously and painfully worked out, and the mortality was high. Nearly all acute cases of appendicitis were complicated by peritonitis: that was the problem, and it was only when the profession finally accepted the teaching of Murphy regarding the wisdom of operating as soon as the diagnosis had been made that improvement came about.

Most of the surgeons were very good, each in his own way. Page was quite brilliant in carrying out the old tradition of rapid, skilful operating. Hume was thoughtful, careful, and deliberate, while Rutherford Morison was outstanding; for not only was he careful and accurate, but he was bold and original, always trying out new methods and endeavouring to improve the art though guided by what was then known of the science of surgery.

Many of the operations were beautifully executed and were faultless in performance, but there were many disappointments, with high mortality. In retrospect one recognizes two main factors: (1) in very many conditions surgical relief was sought at too late a stage, and (2) preparation was totally inadequate. It was quite usual for patients with the most serious conditions to be admitted late one day and to be operated upon the next morning. Similarly, aftercare was often woefully deficient and the problems involved were ill understood.

Teaching

Clinical surgery was well taught in the wards and out-patient departments, and those students who were keen had excellent opportunities; but there was no supervision, and those who chose to go to the devil might do so quite pleasantly without interference.

With many of the staff ward-rounds were not hurried: they often lasted two to two and a half hours, and were thorough and helpful. The chief wanted to know about every case, and the students had the opportunity of getting in close contact with the living case—not only seeing, but examining the patients. Some of the staff merely made a parade of the visit and got through the complete rounds in about an hour; but their following just went out of curiosity or to be seen by the surgeon, who might be an examiner!

Some of the staff—like Rutherford Morison and David Drummond, who were devoted to hospital work—attended post-mortems regularly. These examinations began at noon, and there was often something doing until about two o'clock. Except for the cold in winter it was wonderful, for so often, alas, continuity in clinical work was established in the dead-house.

Surgical handicraft was well taught to dressers by some of the house-surgeons and by those truly wonderful women the sisters, who were kindly bodies, expert at bandaging and in ward work. What an education to put on a long Liston under their guidance, often spurred by their scathing comments. They were splendid examples of their profession, for they knew how to nurse and they did it. Their discernment was wonderful and their prognosis uncanny. They also taught their juniors the really important things about nursing. Fortunately the juniors were then unfettered by a superabundance of lectures or the fear of examinations.

In the education of the student the great failing was in the integration of the subjects. Once an examination was passed it was looked upon as a hurdle surmounted and done with. Chemistry, physics, and biology were soon forgotten, and there was little encouragement to keep up even anatomy and physiology, for their application to clinical problems was not much invoked. This applied less to pathology, but I am afraid the general proposition held true.

Private Practice

Private surgical practice was very different from what it is to-day. Usually the surgeon went to his patient, and that meant a tremendous amount of travelling by train and horse vehicle and at all sorts of times. For town work some of the surgeons used bicycles or walked, but the physicians stuck to their carriages.

A great deal of operative work was done in the homes of the people, and those who really understood the antiseptic technique and would take care over its details could undertake all kinds of cases with confidence. In retrospect I am prepared to reiterate that I have not yet seen the surroundings in which I could not operate with assurance,

provided always that I personally superintended every detail of the arrangements. We relied on the resources of the household for basins, linen, and furniture. Many a baking-bowl acted as a reservoir for Lister's strong mixture in which to soak towels clean from the wash, and usually an ashet (meat dish) did very well as an instrument-tray.

Some surgeons carried a lot of equipment in the way of portable operating table, small stands, basins, dishes, linen, etc., but most of us carried only a Gladstone bag or something rather larger for holding the instruments. The general practitioner usually gave the anaesthetic, and one of his friends sometimes lent a hand as assistant. In emergencies we usually had to manage without a nurse, though when district nurses were available—and did not faint—they were invaluable. Sometimes a "handy body" had to suffice, or we did without.

In the chloroform days the anaesthetic might be an anxiety, but as often as not this was because the administrator was too timid and the patient would not relax or would want to get off the table. At night illumination was a great trouble : a single gas flame or an oil lamp is a really poor source of light, and no one knows how feeble is the light from candles unless he has tried to do a strangulated hernia or remove an appendix with their aid.

Nursing-homes were starting, but they were just homes, and at that time none was properly equipped for the purpose. That is why so many surgeons were driven to set up their own private hospitals, thus adding to their responsibilities and anxieties.

THE CHANGING FACE OF MEDICINE*

BY

Sir ROBERT YOUNG, C.B.E., M.D., F.R.C.P.

Consulting Physician, Middlesex Hospital and the Brompton Hospital

I think it would be safe to state that at no time have such changes in the science, art, and practice of medicine occurred as during that of the last two generations.

It is over sixty years since I was enrolled as a student of the Middlesex Hospital Medical School. Of the hospital and school as it was in 1889 little remains above ground, but they were even then becoming out of date—though some of us still think of them with almost nostalgic affection. The medical and surgical staff, at that time one of the most distinguished in London, came for the most part from other hospitals, only three men educated at the Middlesex being on the list. They were Bland-Sutton, Essex Wynter, and William Hern, then in junior posts, though they all subsequently achieved great, even exceptional, professional distinction. The school had no professors in those days. The lecturer on anatomy was also surgeon to the throat department. The lecturer on physiology, a learned and very lovable man, was more interested in the minute anatomy and evil ways of the blow-fly than in those of the more evolved members of the animal kingdom. There was no special department of pathology. The post-mortem examinations were carried out by one of the assistant physicians as pathologist, and sections were cut and specimens mounted, in a room attached to the museum, by Jonathan Pollard, the technician—a great character much esteemed by the Middlesex men of that period.

*A shortened version of an address given to the Middlesex Hospital Medical Society.

I want here to consider very briefly some of the more important developments which have helped to bring about the chief changes in medical matters. I will begin by a short reference to the textbooks on medicine. The old textbooks, like those of Sir Thomas Watson, a former physician to this hospital, and "Fagge and Pye-Smith" of Guy's Hospital, were descriptive and narrative, with graphic sketches of actual patients, whereas the modern textbooks are systematic and comprehensive. I still sometimes dip into "Fagge and Pye-Smith" for the sheer joy of retrospect and recollection. Each chapter had apposite quotations from the classics or the poets. For example. the description of varicella was prefixed by a quotation from Dryden, "Each little pimple had a tear in it, to wail the fault its riding did commit." While that on one of the painful results of human sexual frailty was introduced by this quotation from *King Lear* : "The gods are just. and of our pleasant vices make instruments to scourge us."

Another change which had influenced the practice of medicine is the improved means of communication. Before motor-car days the staff arrived at the hospital, according to their degree of affluence, in a brougham or Victoria with a pair of horses, or a single-horse brougham, or in the picturesque hansom cab. They came in frock-coats and tall hats. One member used sometimes to drive up in a phaeton and pair with a groom. At one hospital, a friend tells me, one of the surgeons used sometimes to arrive on horseback. The first member of the staff to use a motor-car was, I think, Sir John Bland-Sutton, who arrived in an electric brougham. At another hospital one of the surgeons used an early form of motor-car, which was called by his students the Gumma, because it was always breaking down—a habit which, I gather, the rare examples of gumma have now given up, though the motor has not followed suit to the same extent.

The Clinical Laboratory

Perhaps one of the greatest factors in effecting the changed conditions of the practice of medicine has been the evolution of the clinical laboratory. In my student days, and for some time afterwards, the chief clinical tests were those of the urine, usually carried out in the wards by the house-physician or the clinical clerk. The microscope was chiefly used to identify urinary deposits. Blood counts and haemoglobin estimations were relatively uncommon, and bacteriological examinations a rarity. I think it was in 1899 that Dr. Foulerton was appointed in charge of a department of bacteriology and public health. It was to him and to his assistant, Dr. Hillier, that we began to take our problems with increasing frequency. In 1914, after the foundation of the Bland-Sutton Institute, Professor Carl Browning was appointed its first director.

The help given to medicine and surgery by the discovery of *x* rays by Roentgen in 1895 is almost incalculable. In this hospital the earliest use was the installation of a small coil vacuum tube, costing £14. It was employed for slight casualties of the feet and hands, under the direction of one of the office staff, Mr. C. H. Marsh. In 1902 a temporary building was installed in the courtyard and irreverently called the "Tin House." The first radiologist was Dr. C. R. C. Lyster, a man of great enthusiasm and charm of character. He was assisted by Mr. Mann, previously in charge of the photographic department. Both these men died from the effects of the rays, and were among the earliest victims. The developments in technique since then have been amazing. The whole subject has advanced so rapidly in its developments and applications that it has become necessary to separate radio-diagnosis

from radiotherapy, and in each division there is already advancing specialization.

Advances in Periods

It is of great interest historically to notice how the advances and changes in medicine have been made in periods. We have the age of the description and separation of diseases from their clinical manifestations, from the time of Sydenham, whose descriptions of the fevers and of diseases like gout are classical and epoch-making. Nearer to our own times we have the descriptions by Bright, Addison, and Hodgkin of the diseases to which their names are attached, which left little to be added from the clinical point of view, and more recently the distinction between typhoid and typhus by Sir William Jenner.

The study of morbid anatomy and, later, of morbid histology, of which Virchow was the protagonist, advanced our knowledge of the effects of disease and the topography of disease effects. Sir William Goodhart in 1912 gave the Harveian Oration on "The Passing of Morbid Anatomy." He recognized that we were advancing from the study of disease effects to that of processes and mechanisms. A great impetus was given to this aspect by the applications of bacteriology and the immunity reactions. The evolution of vaccines and serums was a practical result. In more recent years the experimental processes in the laboratory have greatly extended our knowledge of disease and enriched our means of prevention and treatment. I was a member of the Physiological Society when Gaskell was studying the primitive properties of tortoise heart and evolved the five primitive properties of cardiac muscle, and when Burdon-Sanderson and his co-workers were studying the electrical reactions of the heart by means of the string galvanometer. How transcendental they seemed—yet they are the basis of modern cardiology.

Another physiological gift of the greatest value has been the study of the endocrines. I remember that the first time I entered the wards in this hospital as a locum clinical clerk there was admitted a typical case of myxoedema in a woman; but there was no treatment and the woman left the hospital *in statu quo*. A few months later one of the first cases I had in the beds I had to study was a case of myxoedema in a man. He was a cooper working in a street near the hospital. He complained of lethargy, which caused him to make fewer barrels than before. He was given thyroid treatment, which rapidly restored him to functional efficiency. I also remember Schäfer and Oliver working with suprarenal extracts, and how one of them, remembering its vasoconstrictor action, used it to stop nose-bleeding in a young relative. Since then, think of the extent to which the hormones are proving useful in treatment.

Types of Disease

Change in the types and forms of disease in the course of years is, I think, a subject which has been somewhat neglected, though it is of absorbing interest. Space will allow me to refer to only a few of these. Chlorosis was a very common condition in my early years of practice. At out-patients on a Saturday afternoon I often used to see up to four or five new cases and, of course, corresponding numbers of old ones. They were all given Blaud's pills—up to three, three times a day, with aloes pills for obvious reasons. You will see, therefore, that massive doses of iron are no new thing. Chlorosis disappeared when the "living-in" system in big shops was abolished and when women wore hygienic clothing and ceased to tight-lace. I am emphatic, however, that it was a different condition from the hypochromic anaemias you now see, and that it was a clinical entity. Cirrhosis of the liver is now very much less common than in those days. Gout is another disease less often seen nowadays, at any rate in its more tempestuous forms. This may be due to more temperance in diet and alcoholic indulgence, but I wonder if that is all the explanation.

Rheumatic fever is less often seen in the more acute forms as described in textbooks, and I am told that rheumatic nodules, which we regarded as an almost certain indication of serious cardiac involvement, are now rarely seen. Diseases of infective or bacterial origin also seem to vary, sometimes periodically. When I was a student scarlet fever was a serious and much-dreaded disease, with grave complications, like nephritis, otitis, and rheumatism. It seems to be much milder nowadays.

Diseases for which specific or prophylactic treatments have been evolved are also examples of change. The description of lobar pneumonia in textbooks has had to be rewritten, as the classical disease with acute onset, fastigium, and crisis is rarely, if ever, seen since the sulphonamides and penicillin have been introduced, though the sequels and complications still exist and need consideration. Another pathological condition formerly common and now rare is amyloid or waxy disease. I had recently to look up some of the post-mortem records of the Brompton Hospital. In 1890 there were examinations of 114 fatal cases of pulmonary tuberculosis, among which amyloid changes were found in 23 cases—that is, 20%. The marked increase in the cases of bronchial carcinoma is now generally accepted, though, alas, not yet explained.

A special department of medicine which has advanced as much as any during my lifetime is that of tropical diseases and parasitology. The conquest of malaria and of yellow fever has enabled great engineering works to be completed which were previously prohibited by mosquito-borne disease, and has rendered areas previously the "white man's grave" habitable and even salubrious. It is interesting to recognize how much we owe to the study of the life history of ticks, mosquitoes, lice, the tsetse fly, the flukes, and worms. There is, however, one group of diseases which I feel is a grave menace to mankind, and that is the virus group. Viruses are attracting special attention, and so far our knowledge of their life history and mode of action is exiguous, but we may hope that light is slowly being shed in these dark places.

Specialization

Another change in medical practice and treatment has evolved from the modern development of specialization. When I joined the hospital the only special departments were for diseases of the throat and nose, the eye, the skin, and those of women and children. Except for the last two mentioned, there were no special beds, and beds were obtained for special cases only by the courtesy of the physicians and surgeons. Specialism has certainly advanced our knowledge and improved our methods of diagnosis in many diseased conditions. The development and improvement of instrumental methods have been a notable factor in promoting specialization. It was in 1855 that Manuel Garcia, a teacher of singing, invented the laryngoscope. Now we have "scopes" for every orifice and cavity. We take samples of the bone marrow by a drill and explore the cavities of the heart with a cardiac catheter. The advances in the study of physiology, pathology, chemistry, and physics as applied to special departments have also contributed, though there is occasionally a curious time-lag in these applications, as instanced by the use of curare in conjunction with anaesthetics. Public

demand for specialists has also been an important factor. So far specialism has been in the main beneficial, but I fear it may lead to the passing of the general physicians in hospitals, where their value in teaching, and especially in giving a right perspective and in recognizing the importance of considering the patient as a whole and not parts of him, is of the greatest value. I am also afraid that the general practitioner may be deposed from his present position as the guide and trusted friend of his patients, and that not only in medical matters. I would hazard a guess that some of my audience have been influenced in their choice of our profession by the example or the advice of the family doctor.

Clinical Instinct

In the light of this description of the conditions of teaching in my student days and the limitations from which my teachers suffered in comparison with the plethora of assistance of the present time, what is my reaction to their memory? I may say at once, it is that of abiding admiration and gratitude. They used their five senses methodically and remarkably acutely. They insisted on the definite sequence of inspection, palpation, percussion, and auscultation. They seemed to develop what it was the custom to describe as a sixth sense, or clinical instinct—a mind's eye, as I should prefer to call it—which was in fact the summation of the information provided by systematic observation and the recalling of stored memories of other cases. I am convinced that they were, subject to the limitations of knowledge in their day, as often right as the clinicians of the present day. Of course, it is dangerous to rely on clinical instinct only. I feel, and have always felt, that we should use every means to arrive at our diagnosis and to determine the best means of helping the patient, but I hope I shall not be regarded as reactionary when I say that nowadays many patients are over-investigated and over-treated.

In conclusion, though the face of medicine is ever-changing, I trust and believe that the soul or ideal of medicine will remain as it has since Hippocratic days—the patient, the whole patient, and nothing but the patient's interests.

GENERAL PRACTICE FIFTY YEARS AGO

SOME REMINISCENCES

BY

ALFRED COX, O.B.E., LL.D., M.B.

There can be only a handful of men left who entered general practice the way I did—as an apprentice and dispenser-assistant. In the year in which I qualified, 1891, the G.M.C. forbade the employment of unqualified assistants—a wise move, because there were hundreds of dispenser-assistants all over the country in those days, many of whom were grossly exploited, and fewer of whom ever qualified.

In the early nineteen hundreds the habits of the G.P. were being transformed by the advent of the motor-car. Up to that time, unless you were an old-established and therefore privileged practitioner, the top hat and frock-coat were almost *de rigueur*. I have even seen doctors cycling in this uniform. The older and more prosperous men had their smart dogcart or brougham. The younger ones walked or cycled and hired a cab in specially busy times. What we went through in the days when cars were mechanical mysteries, tyres very treacherous, and roads were not macadamed can be imagined. But we persevered under the belief that the car was going to save much precious time. I wonder what we did with all the time saved.

Nearly all doctors dispensed their own medicines, and there is no doubt we had a more intimate knowledge of the drugs we prescribed than is the case now, and we were much less at the mercy of the manufacturing chemist than are the doctors of to-day. I suppose the red lamp which at one time adorned the entrance of most town doctors' houses has quite disappeared. It was even in my time beginning to be regarded as rather bad form. But it had its uses in streets which were poorly lighted when a stranger was looking for a doctor in emergency.

Our practices were largely built up on a reputation for midwifery. My clientele was composed as to 90% of working-class people with large families and small incomes, and our fees were regulated accordingly. It was not unusual for a G.P. to do as many as 150 to 200 cases in a year. This entailed much weary night work, and men grumbled about it. The 1914–18 war saw the transference of much of this work to midwives of an increasingly competent kind. There was more grumbling about that, but there can be no doubt that the change has made the work of the G.P. easier.

I practised in Gateshead from 1891 until 1908, when I joined the staff of the B.M.A. Most of the doctors in Gateshead had family clubs for their poorer patients. A subscription of 3d. a week was collected at their homes by a collector, who was paid a commission but who was not supposed to do any canvassing. But unfortunately canvassing was prevalent in my day and caused a lot of friction between doctors. There were also a good many friendly society appointments in which members could get their doctors' services for 2s. 6d. or 3s. a year. There was quite keen competition for these jobs, as they gave the practitioner an introduction to the family.

It was no secret at the time that many of these friendly society appointments were obtained by bribery and corruption. I put it to some of my colleagues that we ought to get together to find a remedy for this sordid business. Reform, I was convinced, must come from ourselves.

Then "The Battle of the Clubs" began, and a few of us tried to ginger the B.M.A. into taking a more active part in this. Matters came to a head in 1900, when, in response to a proposal put forward by the secretary of the Manchester Medical Guild, there was a conference in Manchester of representatives of many local medical societies and of some branches of the B.M.A. in England and Wales. The third day of that meeting was devoted to medical organization, and many of the Lancashire representatives were in favour of setting up a new body devoted exclusively to medical politics and ethics. I resisted this and moved that "every attempt should be made to capture the B.M.A." It is of interest to record that Smith Whittaker, of Great Yarmouth, who subsequently became the first Medical Secretary of the B.M.A. and later Deputy Chairman of the Board of Insurance Commissioners, said then that "he could not hope that the Association would ever reform itself."

The committee appointed by the conference was invited to meet the Council of the B.M.A. at its Annual Meeting at Ipswich in 1900, and, largely owing to the influence of Sir Victor Horsley, a member of Council, we had an unexpectedly favourable reception. The result was that a constitution committee was appointed. It drew up a report

which was approved by the Annual Meeting of the B.M.A. at Cheltenham in 1901.

What a helpless, unorganized body we were before 1903, when the B.M.A. came alive to its responsibilities to the general practitioner. Before that time nobody thought of the Association as the natural protector of the men who form the bulk of the profession. But it soon tackled the glaring abuses of contract practices and the miserable salaries paid for such posts as parish doctor, just in time to be ready when National Health Insurance plunged us into a great political struggle, the result of which, *inter alia*, was greatly to improve the lot of the average general practitioner.

Since 1914 the change in the financial position of the general practitioner has been phenomenal. I suppose there are few who remember the inquiry made by the Government in 1912, when an independent firm of accountants was directed to find out what the doctors in six towns (selected by agreement with the B.M.A.) actually earned per head of the local population for every kind of medical service rendered. It emerged that the average income of all the doctors (225) whose books were examined was £493 a year, which worked out at 4s. 3d. a head, including every section of the local population.

One thankfully recognizes that the present-day G.P. is able to do much more for his patients than we were. He has many remedies quite unknown in my time, when every pneumonia case was a gamble, as we could only treat symptoms. And nearly every puerperal septic case was a tragedy—perhaps the most painful of any in the practitioner's daily work.

It may come as a surprise to my younger readers to hear that there was a time when patients did not want to go into hospital. Many thought that being sent there was a sign that their complaints were incurable. The word operation was anathema. I understand that nowadays it is only the paucity of hospital beds that prevents the majority of patients from having their illness there. I fancy the G.P. of my time was readier than his successors to tackle minor surgery. We had the idea that our hospital training was intended to make us equal to opening an abscess or dealing with a simple fracture. I am credibly informed that a large proportion of these cases now find their way to hospital. This *may* be all right, but it gives one the impression that much of the elaborate training of the student will be wasted. And I need hardly point out that this state of things does not enhance the reputation of the G.P.

We had one advantage denied to the present generation—at any rate to those entering the National Health Service. We lived in a time when it was regarded as a laudable ambition for a doctor to work hard to build up a practice he could call his own—something he *created* and which accumulated a capital of goodwill with which he could look forward to the future when the time came for retirement. Now, private property of almost any kind is coming to be regarded as nearly a crime against the community. The young G.P. now is working in a practice which belongs to the State, and I doubt if he will put into it the same energy and devotion as we did. But of course I am an old and an old-fashioned man.

But there have been many changes for the better—a great increase in the scientific aspects of practice, with fair hopes of even greater triumphs in the near future. I have even a hope that some day that opprobrium of our profession named very properly the "*common*" cold may be mastered, and I can think of no disease, not fatal, which causes more misery and discomfort.

TRANSPORT AND COMMUNICATIONS

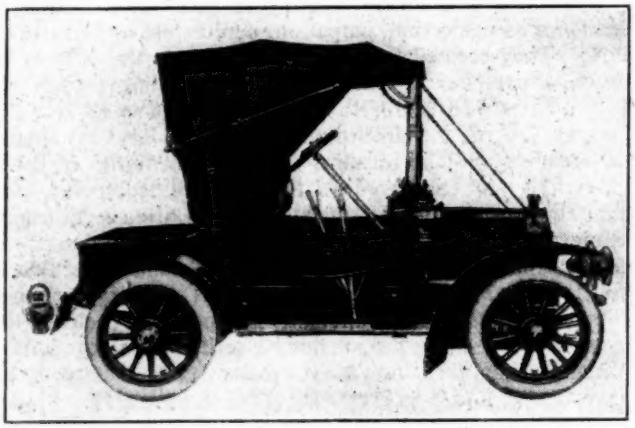
BY

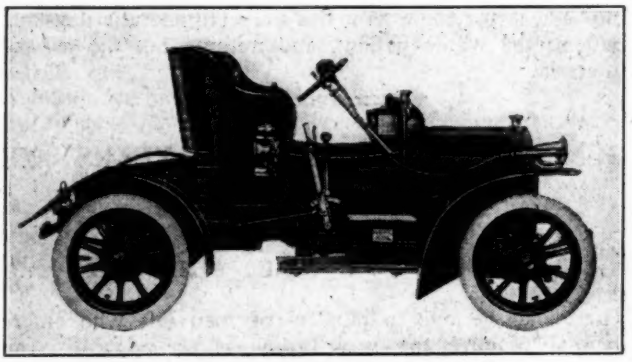
W. J. BISHOP, F.L.A.

Librarian, Wellcome Historical Medical Library

The only outstanding inventions in the field of transport and communications that fall within the twentieth century are the aeroplane and broadcasting. Railways, the telegraph, the telephone, and the motor-car all came in during the Victorian era. But neither the telephone, which dates from 1876, nor the motor-car, which reached England about 1895, came into common use until after the turn of the century.

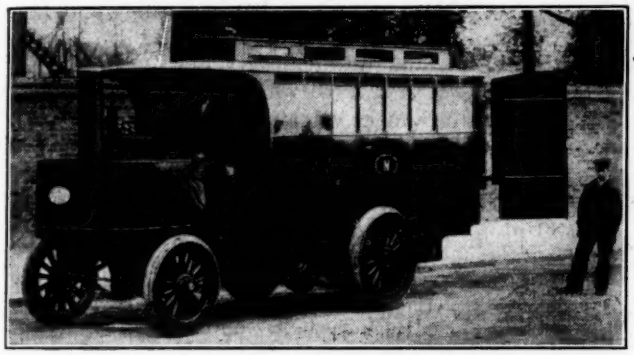
The first great change in the doctor's means of transport since the invention of the wheeled carriage was brought about by the advent of the motor-car. The *British Medical Journal* of May 16, 1896, described an "Exhibition of Horseless Carriages" which showed that "the manufacture of these vehicles is now passing out of the experimental stage." Particularly commended was "a very workmanlike carriage," costing about £125, which was "easily steered and stopped, and did not give out much smell."





Two well-known models popular in 1907

Doctors were the first large professional group to experiment seriously with the car and to keep records of its cost and performance. For example, Sir Henry Thompson, the celebrated surgeon, was one of the pioneers of motoring in England. In 1902 he contributed a chapter on "Motor-Cars and Health" to the volume on *Motors and Motor-Driving* in the Badminton Library, and recorded



Steam-driven ambulance, 1902

that at the age of 82 he was in the habit of making journeys almost daily in his automobile.

Charles Barrett Lockwood is said to have been the first member of the staff of St. Bartholomew's to drive to hospital in his own car—about 1905. This was painted a bright scarlet and was known as "The Red Peril." In 1906 Lockwood was chairman of a "Committee of Medical Men who are Users of Motor Cars." Although the medical profession took rapidly to the use of the motor-car, advertisements of horses and horse-drawn vehicles persisted in the *British Medical Journal* and elsewhere almost up to the time of the 1914–18 war.

The mechanization of ambulances began in this country in 1902, when a steam ambulance car was put into commission by the Metropolitan Asylums Board. This vehicle accommodated eight stretchers and was capable of a speed of five miles an hour. The first ambulance to be driven by an internal combustion engine was manufactured in 1904 and had many unique features. It could carry only one stretcher case, but had a speed of fifteen miles an hour. Horse ambulances were finally abandoned by the M.A.B. in September, 1912. At the present time the London County Council is the largest user of civil ambulances in the world, with 150 petrol-driven vehicles.

From Kitty Hawk to Cloncurry

The possibility of a new method of evacuation of casualties was recognized very soon after the Wright brothers made their historic flight over the sand dunes of Kitty Hawk in 1903, but there is no clear record of the transportation of wounded by air until 1915. Then during the Serbian retreat Captain D. Angelzer and Lieutenant Paulhan, of the French Air Service, carried twelve wounded men distances of 80 to 200 kilometres using service-type planes. To these two Frenchmen is due the honour of having given a literal meaning to the term "Ambulance Volante" used by their countryman Baron Larrey in 1792.

While attached to the R.F.C. in Egypt in 1917, the late Major Alexander Dingwall Kennedy, R.A.M.C., had a D.H.9 converted for the accommodation of stretcher cases. An improved model of the same machine was used in 1919, when three patients were moved 175 miles to base in the short air war against the "Mad Mullah" of Somaliland.

The first aerial ambulance built for the Royal Air Force was a Vickers-Vimy twin-engined machine constructed at Weybridge in 1920, but air evacuation was first used on an appreciable scale in Iraq in 1923.

In 1941 there were 1,996 patients transported by air, most of them during Wavell's advance in the Western Desert; in 1942 just over 10,000 patients, and in 1943 a further 40,000, were carried by air. The peak of effort was realized in 1944, when about 300,000 sick or wounded were removed by air on all fronts, without a single mishap. Between D Day on June 6, 1944, and VE Day on May 8, 1945, the R.A.F. evacuated 77,348 patients to the United Kingdom from the Continent. This was slightly more than the number taken by the sea route.

Although less spectacular, the services which aviation has rendered to medicine in times of peace are as noteworthy as those given in war. The aeroplane enables medical aid, drugs, vaccines, and sera to be carried to the scene of any epidemic or disaster in the shortest possible time. Patients can be safely transported for special treatment in any emergency; consultants can fly from one end of the world to the other in as many hours as it would have taken weeks or months fifty years ago.

The story of the Australian Aerial Medical Services provides one of the most striking examples of the benefits conferred by the conquest of the air. Over 1,380,000 square miles of the Australian hinterland there is no settlement large enough to support a resident doctor. Many settlers are hundreds of miles from the nearest medical man.

The Queensland and Northern Territory Aerial Service owed its inception to the Rev. John Flynn, of the Australian Inland Mission, and was inaugurated in 1928, having its base at Cloncurry in North-west Queensland. An essential factor in this "Flying Doctor" scheme is the provision of simple wireless sets which derive their power from small high-tension generators worked by bicycle pedals. The "Mother Station" is in daily contact with some forty pedal "Transceivers" distributed among the settlers. The "Flying Doctor" flies on an average 20,000 miles a year and attends directly about 250 patients. The service was placed on a national basis in 1934, and as the Australian Aerial Medical Services, which is a Commonwealth Body, it enjoys Federal and State government assistance.

Turning to transportation in a purely vertical direction it may be noted that the first passenger "elevator" was invented by Elisha Graves Otis in 1857. The first successful electric lift was installed in New York in 1889. Many hospitals in Great Britain had lifts fitted before the end of the last century, although many of them were very primitive affairs, and the earliest models were often constructed in skeleton cages entirely outside the main building.

London County Council Ambulance, 1949

Electric Messages

The first practical telegraph was invented by Morse about 1832–5. One of the best-known early instances of its use was during the Prince of Wales's attack of typhoid in 1871, an occasion commemorated by a later poet laureate:

> "Across the wires the electric message came:
> 'He is no better, he is much the same.'"

The *British Medical Journal* in 1880 hailed telegraphy as "an inseparable part of modern arrangements for life," and made a strong plea for the provision of telegraphic facilities at all hours of the day and night. During August, 1883, the *Medical Record* of New York provided its readers with telegraphic summaries of the daily proceedings of the British Medical Association's annual meeting at Liverpool. Congratulating his American contemporary on this achievement, the Editor of the *British Medical Journal* pointed out that free use of the cable for obtaining medical information was by no means new. Cabled reports of the cholera epidemic in Egypt had appeared in the *B.M.J.* in July, 1883.

An editorial on "Therapeutics by Telegram" in the *British Medical Journal* of April 29, 1893, inveighs against the ubiquitous agents of the daily press who were constantly announcing by telegraph the discovery of some wonderful cure. Among the recent cases cited was the telegraphic statement that Professor Koch had discovered a new and infallible cure for tuberculosis.

The telephone was invented by Alexander Graham Bell in 1876, and in 1878 the first telephone switchboard for commercial subscribers was put into operation at New Haven, Connecticut, with twenty subscribers. It is a striking fact that when the telephone first came into use it commended itself to the medical profession mainly as an aid to physical diagnosis. Thus the *Boston Medical and Surgical Journal* in 1878 discussed "its utility in the class demonstration of auscultative signs."

In medical circles in England the telephone was at first hailed as a means of communicating with patients suffering from infectious diseases. The *British Medical Journal* of May 11, 1878, states that "it has been in use in the house of a medical man during the last few weeks, to enable a member of the family suffering from an infectious exanthem to communicate with her family and friends; and this application we would recommend as very practical to the managers of fever-hospitals and asylums."

Soon afterwards some doctors began to advertise the fact that they could be summoned or consulted by telephone by day or night, and this led to charges of unprofessional conduct. Many medical men thought that the telephone was not sufficiently private, and pointed out the dangers to be feared from eavesdroppers.

Marconi came to England in 1896 and on June 2 took out the first patent ever granted for wireless telegraphy based on the use of electric waves. In March, 1898, he established communication across the English Channel, and on December 12, 1901, succeeded at his first attempt in transmitting and receiving signals across the Atlantic. The medical applications of wireless came more rapidly than those of the telegraph and the telephone. In July, 1898, the Prince of Wales, while staying at Waddesdon with Baron Ferdinand de Rothschild, fell and fractured his patella. He was attended on the Royal yacht *Osborne* by Mr. (later Sir Alfred) Fripp, and at Cowes "an unknown Italian called Marconi came on board and astonished the world by sending daily bulletins of the Prince's progress by wireless to Queen Victoria at Osborne House." By the end of 1899 communication between ships and land stations over distances of 80 to 100 miles became an accomplished fact, and within a very few years all large ocean-going vessels were fitted with Marconi's apparatus.

Wireless soon proved its value in cases of shipwreck and fire, and from the early years of the present century we read of shipmasters requesting and receiving by wireless professional advice on the treatment of accidents, the management of labours, and on medical and surgical emergencies of all kinds.

We are indebted to Sir Allen Daley for the photographs of the L.C.C. ambulances. The pictures of cars popular in 1907—a 7 h.p. Singer and a 10–12 h.p. Humber—are taken from the *British Medical Journal* of May 4, 1907.

PICTORIAL SUPPLEMENT

ACKNOWLEDGMENTS

In the preparation of the twelve pages of pictures which accompany this special number of the *Journal* help was given by a number of advisers whose assistance is here gratefully acknowledged. Many medical men and women went to much trouble to provide photographs which had finally to be excluded because of lack of space.

We are especially indebted to the following: Professor G. Grey Turner for the photograph of Rutherford Morison operating; Dr. Paul Wood for the direct-writing E.C.G. of a case of right bundle-branch block; Professor Samson Wright for the electromyograph and electroencephalograph tracings; Dr. A. S. McFarlane for the electron photomicrographs of influenza virus and *M. tuberculosis* (avian), which appeared originally in the *Journal* of December 3, 1949, and Dr. I. M. Dawson, lately of the National Institute for Medical Research, for those of *Staph. aureus* and *Bact. coli*; Professor V. Du Vigneaud, Department of Biochemistry, Cornell University Medical College, New York, and Dr. F. Prescott, of the Wellcome Research Institution, for photographs of vitamin crystals; Dr. F. M. Allchin for photographs of the 10-gramme radium unit at the Westminster Hospital; Professor W. V. Mayneord for photographs of the synchrotron at the Royal Cancer Hospital, Fulham; Dr. S. Cochrane Shanks for the photograph of the *x*-ray diagnostic department at University College Hospital and the print of the radiograph taken by J. Norman Collie in 1896; Dr. J. R. Busvine, of the London School of Hygiene and Tropical Medicine, for photographs of D.D.T. and gammexane crystals; Dr. G. M. Komrower for photographs of the "perspex" oxygen tent originally described in the *Journal* of May 28, 1949 (p. 953); Dr. E. Ashworth Underwood and the Wellcome Historical Medical Museum for the picture of Mackenzie's polygraph; Mr. S. L. Barron for the electrocardiogram made by Sir Thomas Lewis; Mr. F. C. Grigg, the Honorary Curator of the Royal Microscopical Society, for the photograph of a microscope in use in 1900; Mr. G. S. Innes and the Department of Medical Photography at St. Bartholomew's Hospital for photographs of the million-volt therapy unit.

Certain individual illustrations were reproduced, or in some cases redrawn, from the following books: *The Study of the Pulse*, by Sir James Mackenzie, 1902, Y. T. Pentland, Edinburgh; *An Atlas of Bacteriology*, by C. Slater and E. J. Spitta, 1898, Scientific Press London; *Vitamins in Medicine*, by F. Bicknell and F. Prescott, 1946, William Heinemann (Medical Books), Ltd., London; *Insects of Medical Importance*, by John Smart, 1943, British Museum, London; *Pathology*, by J. M. Beattie and W. E. Carnegie Dickson, 1948, fifth edition, William Heinemann (Medical Books) Ltd., London; *Pneumotherapy*, by P. L. Tissier, 1903, Rebman, Ltd., London; *Blood Transfusion*, by V. H. Riddell, 1939, Oxford University Press, London; *History of the Birmingham Medical School*, 1925, Cornish Brothers, Birmingham.

Two of the older pictures on page 7 are taken from an article by J. Battersby in the *Archives of the Roentgen Ray* (1899, 3, 74) and from an article by A. D. Reid in a special number of the *Practitioner* (1906, p. 80). The Einthoven tracing is from the *Archives Néerlandaises des Sciences Exactes et Naturelles* (1904, 9, 202).

Photographs of some of the crystals of hormones, vitamins, and antibiotics, and of different manufacturing processes, were kindly supplied by: Boots Pure Drug Co., Ltd.; Burroughs Wellcome and Co.; Ciba Laboratories, Ltd.; Glaxo Laboratories, Ltd.; I.C.I., Ltd.; Lederle Laboratories; Parke, Davis and Co.; and Roche Products, Ltd.

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